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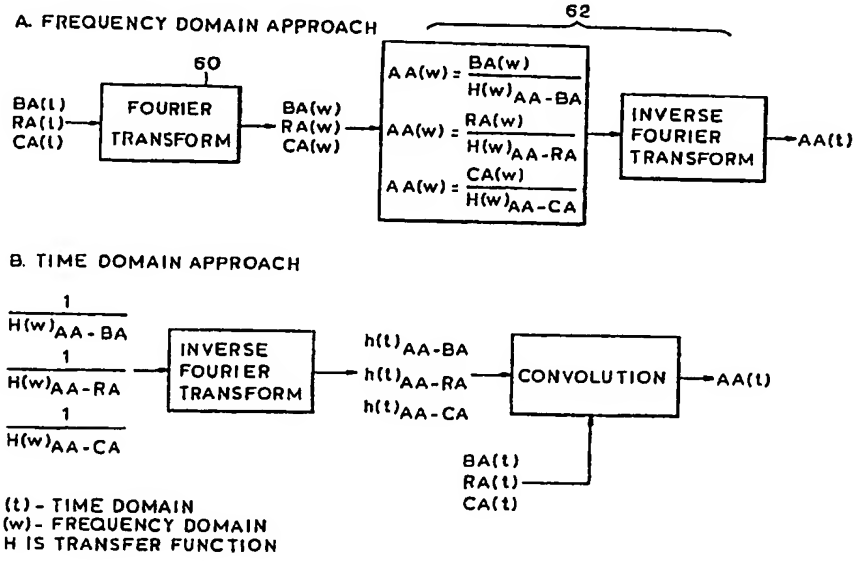
(57) Abstract

The invention is a method for calculating from the contours of the pressure pulses in the brachial, carotid and radial arteries the absolute systolic pressure, the degree of augmentation, and the contour of the pressure pulse wave in the ascending aorta. The pressure in the ascending aorta is related to a combination of a primary pressure pulse and a secondary pressure wave which is a reflection of the primary pressure pulse from the periphery of the body. The maximum central arterial pressure can be determined from an analysis of the contour of the pressure pulses in the peripheral arteries, and the relationship between the peaks in the pulses relating to the maximum primary pressure and the maximum secondary wave pressure. The inventive system determines the positions of the two peaks and then analyses their amplitudes to ascertain the maximum systolic pressure in the central arteries and the amount of augmentation. Transfer functions relating the measured peripheral artery pressure pulses to the ascending aorta pressure pulses developed from an analysis of the pressure pulse waves of a number of individuals using Fourier transform techniques are used to determine the contour of the ascending aorta pressure pulse based on the measured peripheral pulses.



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A METHOD AND APPARATUS FOR ASCERTAINING THE CONTOUR OF THE PRESSURE PULSE IN THE CENTRAL ARTERIES FROM THE CONTOUR OF THE PRESSURE PULSE IN THE PERIPHERAL ARTERIES

This application is a continuation in part of the application serial no. 07/464,890 filed January 16, 1990, which is a continuation in part of the application serial no. 07/328,285 filed March 24, 1989.

Background

The contour of the central arterial blood pressure pulse of an adult is different from the contour of the pressure pulse of a youth. The pressure pulse of an adult has an augmented peak in late systole, and a near-exponential decay during diastole, while the pressure pulse of a youth has a rounded peak throughout systole and a second peak during diastole.

The differences in the two pressure pulse patterns are attributable largely to an early return in an adult of a secondary reflection wave, that is, a reflection of the primary pressure pulse along the arterial tree from the periphery of the body. The early return of the secondary wave is due to an increase in the velocity of the arterial pulse caused by a stiffening and/or mismatch of the conduit arteries in the adult. Because of its early return, the secondary wave arrives at the heart during, and thus augments, the systolic peak of the pressure pulse.

A youth has arteries which are more elastic, and therefore, the arterial pulse wave is slower in the youth than in the adult. Thus the secondary wave does not return as early in the pulse cycle, and therefore, it does not combine with, or augment, the systolic peak of the central pressure pulse. Instead, the pulse has a second peak in diastole which corresponds to the later return of the secondary wave.

With increasing age, characteristic changes can be seen in the contour and amplitude of the pressure pulse in both the central and the peripheral arteries, due largely to the earlier

return of the secondary (reflected) wave. From the fourth decade on, a relatively large augmentation of the pulses in late systole can be observed in the carotid artery and ascending aorta. Such augmentation is not observed, or not observed to the same degree, in the pulses in the peripheral arteries, however, until the eighth decade. Thus measurements of blood pressure in the peripheral arteries are not completely accurate representations of the pressure in the carotid artery or ascending aorta.

The discrepancies in pressure between central and peripheral arteries help to explain why, in arterial hypertension, the degree of arterial damage and the severity of left ventricular hypertrophy do not always correlate well with the level of brachial systolic pressure. The discrepancies also explain why regression of left ventricular hypertrophy induced by various drugs does not always accord with the degree of reduction in brachial arterial pressure.

The usual clinically-accepted method for determination of the condition of the left ventricle in man is through measurement of systolic arterial pressure in the brachial artery with a sphygmomanometer. The clinician then uses the measured systolic pressure as an indication of the pressure in all major arteries of the body. Such an assumption is not justified, however, because of the differences in the effect of wave reflection in the periphery of the body and the central arteries, as discussed above.

While these problems with blood pressure interpretation are generally known, no one has previously developed a noninvasive measurement method which is more accurate than the sphygmomanometer for assessment of central aortic pressure. Yet it is highly desirable to be able to ascertain augmentation of pressure pulses in the ascending aorta from an analysis of the contour of the primary and secondary pressure waves in

peripheral arteries. This would allow physicians to diagnose and treat more appropriately abnormal blood pressure and arterial conditions early in life, and thus, aid the physicians in pre-empting the dangerous effects of such conditions in later life.

Summary of the Invention

The invention is a method for calculating from the contours of the pressure pulses recorded invasively or noninvasively in the brachial and/or radial arteries both the degree of systolic pressure augmentation and/or the absolute systolic pressure in the ascending aorta and the left ventricle.

The pressure in the ascending aorta is related to a combination of the primary pressure pulse and the secondary pressure wave which is a reflection of the primary pressure pulse from the periphery of the body. Measurement of the pressure at the peripheral arteries does not alone provide an accurate figure for the maximum systolic pressure in the central arteries, for example, in the ascending aorta. Analysis of the pressure wave in the peripheral arteries can provide indirect measurement of the maximum systolic pressure in the central arteries. In particular, the maximum central arterial pressure can be determined from an analysis of the contour of the pressure pulses in the peripheral arteries, and the relationship between the peaks in the pulses relating to the maximum primary pressure and the maximum secondary wave pressure. The positions, and thus the amplitudes, of the two peaks are not always readily apparent from a visual inspection of the pulse contour, particularly when the secondary wave returns early in systole. Thus the inventive system first determines the positions of the two peaks and then analyses their amplitudes to ascertain the maximum systolic pressure in

the central arteries and the amount of augmentation.

In brief summary, the inventive system measures the pressure pulses in a peripheral artery either noninvasively using a tonometer or invasively using a conventional intra-arterial device. Either method of measurement produces an electrical signal representative of the contours the pressure pulses. The system digitizes and averages the signal to form an "average pulse." From this average pulse, the system determines the amplitudes of the two pressure peaks by taking various derivatives of the pulse as set forth in the detailed description.

Once the system finds the two peaks, it calculates a reverse shoulder index (RSI) by dividing the amplitude of the second peak by the amplitude of the first peak. If this quotient, or RSI, is greater than an imperically determined maximum it indicates that the central arterial pressure is augmented. The system determines, as a percentage, the amount of central augmentation, that is, a central augmentation index "AI", using one of the following formulas:

From Brachial Pulse	AI = 70 +0.79*RSI
From Radial Pulse	AI = 95 +0.57*RSI

The index indicates how much of the maximum systolic pressure in the central artery is related to the effects of the secondary wave.

The system calculates the maximum central arterial pressure, CP, (in mm Hg) from the amplitude of the secondary wave peak using one of the following formulas:

From Brachial Pulse	CP = 28.6 +0.82*P_{ss} (mm Hg)
From Radial Pulse	CP = 41.3 +0.77*P_{ss} (mm

Hg)

Where "P_{ss}" is the pressure of the second shoulder in the brachial or radial artery pressure pulse.

An augmentation index over "100%" indicates that the maximum central artery systolic pressure, CP, may be reduced, and often substantially, by the administration of drugs which dilate the arteries and reduce wave reflection. To determine the effects of the drugs, a physician can compare the AI and CP values calculated from pressure measurements taken before with the values calculated from pressure readings taken after the administration of the drugs.

BRIEF DESCRIPTION OF THE DRAWINGS

This invention is pointed out with particularity in the appended claims. The above and further advantages of this invention may be better understood by referring to the following description taken in conjunction with the accompanying drawings, in which:

Figure 1 is a diagram of the blood flow and pressure pulses in the ascending aorta, which depicts pressure pulses for both young and old persons;

Figure 2 is a graph of the distribution of aortic pressure wave velocity as a function of age;

Figure 3 is a diagram of radial and carotid arterial pressure pulses at various ages;

Figure 4 is a diagram of the pressure waves in the ascending aorta and brachial artery before and after treatment with nitroglycerine;

Figure 5 is an illustration of an average brachial artery pressure pulse of a youth and the first and third derivatives of the pulse;

Figure 6 is an illustration of an average brachial

artery pressure pulse of an older subject and the first and third derivatives of the pulse;

Figure 7 is an illustration of the ascending aortic pressure pulse corresponding to the brachial artery pressure pulse shown in Figure 6 and the first and third derivatives of the pulse;

Figure 8 is a flow chart for determining the locations of first and second shoulders in the average pressure pulses shown in Figures 5 and 6;

Figure 9 is a flow chart for determining the central aortic pressure from the peripheral pressure pulse;

Figures 10 and 10a are graphs of the distribution of aortic systolic pressure as a function of radial artery second shoulder pressure and of brachial artery second shoulder pressure, respectively;

Figures 11 and 11a are graphs of the distribution of augmentation indices associated with aortic pressure as a function of the augmentation indices associated with radial pressure and with brachial pressure, respectively.

DETAILED DESCRIPTION

I. Pressure Measurements

Figure 1 illustrates, for a heart blood pumping cycle, ascending aortic pressure and blood flow velocity in a relatively young person (type B or C, dotted lines) and an older person (type A, solid lines). Curve 1 represents an EKG reading of a number of heart blood pumping cycles. Curves 2 and 3 represent aortic pressure and blood flow velocity, respectively, during the systolic and diastolic portions of one pumping cycle.

The dotted-line portion of curve 2, which corresponds to

an aortic pressure pulse of a youth, illustrates a non-augmented pressure pulse. The pulse has a maximum peak 4c in early systole, a smaller secondary wave peak 5c in late systole, a dicrotic notch 6 at the onset of diastole and a gradual decay during diastole. The blood flow associated with this non-augmented pressure wave is shown by the dotted-line portion of curve 3. Accordingly, blood flow velocity is at a relative maximum when the associated pressure wave is non-augmented.

The solid-line portion of curve 2, which corresponds to an aortic pressure pulse of an older subject, illustrates an augmented pressure pulse. The pulse has a peak 4a in early systole, an augmented secondary wave peak 5a in late systole, a dicrotic notch 6 at the onset of diastole and near exponential decay during diastole. The corresponding blood flow velocity is shown by the solid-line portion of curve 2. The blood flow in an older subject is seen to be slower than in a youth, while the aortic pressure required to force the blood to flow in the older subject is greater.

Figure 2 illustrates the change in arterial pulse wave velocity with age. This change, which is attributable to a stiffening of the arteries with age, explains why the secondary wave peaks 5a and 5c (Figure 1) occur for the youth and the older subject at different times during late systole. The secondary wave returns earlier in the older subject and it combines with, and thus augments, the systolic pressure peak.

Figure 3 illustrates the characteristic changes in the contour of pressure pulses in the radial and carotid arteries over eight decades. The pressure pulses in the carotid artery are almost identical in shape to the pressure pulses in the ascending aorta. Late systolic augmentation is observed in the pressure pulses in the carotid artery from the fourth decade on. Such augmentation is not readily observed in the radial

artery until the eighth decade.

Figure 4 illustrates an invasively measured ascending aorta pressure wave 7 and a corresponding pressure wave 8 in the brachial artery of an older subject, both before and after the subject ingests nitroglycerin (GTN). The pressure waves labeled "control" correspond to the pressures before the ingestion of the GTN and the waves labeled "GTN" correspond to the pressure after the ingestion of the GTN.

Referring now to the "control" waves, the brachial artery pressure wave 8 includes a series of pulses, each of which has a peak 4a in early systole and a secondary wave peak 5a which correspond to the peaks 4a and 5a of Figure 1. The peak 5a in the brachial artery pulse indicates the return of the secondary wave in late systole. The points labeled S and D, that is, the maximum and minimum points, of the brachial artery pressure wave correspond with systolic and diastolic sphygmomanometer measurements of blood pressure.

When GTN is administered, it dilates the arteries, and thus, it slows the primary pressure wave and also slows and markedly diminishes the reflected or secondary wave. Accordingly, the point labeled R on the brachial artery curves corresponding to the reflected wave is displaced downward and slightly to the right in the GTN curves. Due to the reduced amplitude of wave reflection and to its later return, the aorta does not experience as much pressure from this effect, and thus there is a noticeable reduction in the maximum pressure peak of the ascending aorta pressure wave.

While the reduction in amplitude and later arrival of the secondary wave results in a change in the shape or contour of the corresponding brachial artery pressure wave, the maximum pressure peak, labeled S, is not changed. Accordingly, the sphygmomanometer registers the same systolic pressure reading after the ingestion of GTN as before. Thus it does not

register the effects of the GTN.

2. Formulating Ascending Aortic Pressure From Peripheral Pressure Measurements

As explained above, the effects of the GTN are noticeable in the reduction of the peak pressure in the ascending aorta, which can be directly measured using invasive systems. The effects are also noticeable in changes in the contour of the brachial artery and radial artery pressure waves, which can be measured either noninvasively using a tonometer or invasively through an intra-arterial cannula. The present invention derives the ascending aortic pressure from measurements of the peripheral pressure.

Figures 5-8 depict the steps which the inventive system performs in ascertaining pressure wave augmentation in the ascending aorta. Figures 5 and 6 illustrate graphically the method of determining from the peripheral pulses if the aortic pressure is augmented, Figure 7 illustrates graphically the method of determining from the aortic pressure pulse if the aortic pressure is augmented, and Figure 8 is a flow chart of the steps performed by conventional processors (not shown) in ascertaining pressure wave augmentation.

Figures 5 and 6 illustrate peripheral artery pressure pulses 16 and 17, respectively and Figure 7 illustrates ascending aorta pressure pulse 20. Each pulse has two peaks, a primary pressure peak, labeled "1st shoulder" and a secondary pressure wave peak, labeled "2nd shoulder." The relative amplitudes of the two peaks are analyzed to ascertain the amount of ascending aortic pressure augmentation.

Before the two peak amplitudes can be analyzed, they must be located. First, the start of the pulse, that is, the onset of systole must be found. Then the relative maximum points of the pulse must be located. These points can be found

by analyzing the first derivative of the pulse, which is curve 18. The pulse relative maximum (and minimum) points correspond to the zero crossings of the first derivative curve 18. The maximum point of the first derivative curve corresponds to the point of maximum pulse slope, that is, the point in early systole at which the pulse is rising to its first peak. The point of systolic onset corresponds to the first negative-to-positive zero crossing which precedes the first derivative maximum point. The first derivative maximum point is labeled "MAXdp/dt" in Figures 5-7.

Once the point of systolic onset is located, the absolute maximum pulse point is determined. This is the point which corresponds to the point labeled S in Figure 4, that is, the maximum systolic pressure. It is labeled SMAX in Figures 5-7. The maximum point, SMAX, may or may not correspond to the first peak of the pressure pulse. In order to positively identify the first pulse peak, a third derivative is taken, as illustrated by curve 19. The third derivative curve 19 has a relative maximum at the location which corresponds to the first pulse peak. This relative maximum point is labeled "MAX3rd" in Figures 5-7.

If the MAX3rd point corresponds to the SMAX pulse point, then the pulse has the shape shown in Figures 5 and 6. If the maximum point does not correspond to the SMAX point, that is, if the MAX3rd point location precedes the location SMAX point, the pulse has the shape shown in Figure 7. Referring again to Figures 5 and 6, if the first peak or shoulder corresponds to the SMAX point, the second shoulder is located by finding the first negative-to-positive zero crossing 22 of the third derivative 19 after the MAX3rd point.

If the first shoulder does not correspond to SMAX, as in the pulse shown in Figure 7, the second shoulder corresponds to SMAX. Thus the first shoulder is located at the pulse point

corresponding to the MAX3rd point and the second shoulder is located at the SMAX point.

Once the first and second shoulders are determined, the amount of augmentation can be ascertained by comparing (i) the amplitude of the second shoulder, measured above the amplitude of the pulse at systolic onset, with (ii) the amplitude of the first shoulder, measured above the amplitude of the pulse at systolic onset. If the ascending aortic pressure is augmented this ratio is outside of an imperically determined percentage and the amount of augmentation is related to the quotient of the amplitudes. The computation of the amount of augmentation is explained in more detail below with reference to Figure 9. The amplitude of the second shoulder is also related to the maximum central pressure, as explained with reference to Figure 9.

Figure 8 is a flow chart for determining the locations of the first and second shoulders of the peripheral artery pressure pulse. The various calculations are performed by one or more processors, which are of conventional design. First, a tonometer or an intra-arterial cannula (not shown) measures the contour of the pressure wave in a peripheral artery, for example, in the radial artery. The tonometer or cannula produces an analog wave form which it applies to a processor which digitizes, filters, and averages it by pulses to form an average pulse signal. If a tonometer is used and its calibration is unknown, the processor normalizes the average pulse to the systolic and diastolic pressure readings of a sphygmomanometer.

The processor then finds the pulse maximum point, SMAX (step 24). Next, the processor takes the first derivative of the average pulse and locates the maximum point, MAXdpdt. It then locates the point of systolic onset by finding the first negative-to-positive zero crossing of the first derivative

curve 18 (step 26).

The processor next takes the third derivative of the pulse and locates the MAX3rd point, which is the first relative maximum point of the third derivative which succeeds the MAXdpdt point (step 28). If the MAX3rd point is later in time than the systolic maximum point, SMAX, it indicates that the pulse has a shape which is associated with the Type B or C pulses shown in Figures 1 and 5-6 (steps 30-34). If the MAX3rd point precedes the SMAX point, it indicates that the pulse has a shape which is associated with a much older subject, or the Type A pulse shown in Figures 1 and 7 (steps 32 and 36).

The processor may use an alternative method to determine the type of pulse. It may locate the first positive-to-negative zero crossing point 20 (Figures 5-7) of the third derivative curve 19 which occurs after the MAXdpdt point, and compare the time of occurrence of this point 20 with the time of occurrence of the SMAX point. If point 20 occurs later in time than the SMAX point, it indicates that the pulse is a Type B or C pulse. Otherwise, it indicates that the pulse is a Type A pulse.

If the pulse is Type B or C, the processor equates the first shoulder point, which is the point associated with the peak of the primary pressure wave, with the SMAX point. It also equates the second shoulder, which is the point associated with the return of the secondary or reflected wave, with the pulse point which corresponds to the first negative-to-positive zero crossing point of the third derivative curve 19 which occurs after the MAX3rd point (step 34) as shown in Figures 5 and 6.

If the pulse is a Type A pulse, the processor equates the first shoulder with the pulse point which corresponds to the MAX3rd point of curve 19, and the second shoulder with the SMAX point as shown in Figure 7.

Referring now to Figure 9, once the first and second shoulders of the pulse are identified (steps 40-46), the processor determines if the pulse has an augmented peak. First the processor generates a Reverse Shoulder Index ("RSI") by dividing (i) the pressure at the second shoulder minus the pressure at systolic onset, by (ii) the pressure at the first shoulder minus the pressure at systolic onset (steps 48-50). The RSI is expressed as a percentage, and thus, the quotient is multiplied by 100.

If the RSI is less than a predetermined minimum value, 9% for radial or 38% for brachial in the preferred embodiment, it indicates that the pulse is associated with non-augmented aortic pressure (steps 52 and 52a). If the RSI is greater than the appropriate predetermined minimum value, the pulse is associated with augmented aortic pressure.

If the RSI value indicates that the pulse is not associated with augmented central pressure, the processor next calculates central pressure, CP, by substituting the pressure associated with the second shoulder, P_{SS}, into the appropriate formula (steps 56 and 56a):

$CP = 41.3 + 0.77 * P_{SS}$ (mm Hg) (1) From the radial pulse

$CP = 28.6 + 0.82 * P_{SS}$ (mm Hg) (1a) From the brachial pulse

where "*" indicates multiplication and the numerals 41.3 and 0.77 are the y-intercept and the slope, respectively, of a line corresponding to the best estimate of data presented in a graph of aortic systolic pressure versus radial artery second shoulder pressure as shown in Figure 10, and the numerals 28.6 and 0.82 are the y-intercept and slope, respectively, of a line corresponding to the best estimate of data presented in a graph of aortic systolic pressure versus brachial artery second shoulder pressure as shown in Figure 10a.

The data in Figure 10 and 10a were collected invasively from a number of patients and the values in formulas 1 and 1a represent best estimates of the data. These values may change as more data become available. Similarly, the values of the minimum RSI's associated with augmentation were determined from invasively collected data. These values may change, also, as more data become available.

If the RSI value indicates that the pulse is associated with augmented central aortic pressure, the processor generates an augmentation index, AI. The AI corresponds to a comparison of the amplitude of the secondary wave to the amplitude of the primary wave. If AI exceeds "100%" it indicates that the secondary wave exceeds the first, and thus, that early wave reflection is boosting aortic and left ventricular peak pressure. To calculate the AI, as a percentage, the processor substitutes the appropriate RSI value into one of the following formulas (steps 54 and 54a):

$$AI = 95 + 0.57*RSI \quad (2) \text{ From Radial}$$

$$AI = 70 + 0.79*RSI \quad (2a) \text{ From Brachial}$$

where "*" indicates multiplication and the numerals 95 and 70, and 0.57 and 0.79 are the y-intercepts and the slopes, respectively, of lines corresponding to the best estimates of data presented in graphs of augmentation indices of the aortic pressure versus radial artery and aortic pressure versus brachial artery pressure, as shown in Figures 11 and 11a, respectively. The data for Figures 11 and 11a were calculated from pressures measured invasively in a number of patients. The values in formulas (2) and/or (2a) may change as more data become available.

The processor then calculates the central pressure

corresponding to the augmented pulse using formula (1) or (1a) as appropriate. The central pressure can be similarly calculated from the pressure in the brachial artery. The differences between such a calculation and the calculation depicted in Figure 9 are the y-intercepts and slopes of the central pressure and augmentation index formulas which can be calculated from invasively measured data.

The current invention enables a doctor to accurately determine noninvasively the peak systolic pressure in the ascending aorta. Thus a doctor may monitor noninvasively the effects of medication, exercise, etc. on the systolic blood pressure in the left ventricle of the heart. Before the current invention, a doctor could not easily measure such effects. Thus the doctor could not gauge appropriately medication or other treatment.

The contour of an ascending aortic pressure pulse can be synthesized from the peripheral pulse contour. Referring now to Figure 12, a transfer function processor 58 develops transfer functions relating peripheral pressure pulses and ascending aortic pressure pulses. The transfer function processor 58 accumulates both contours from a number of individuals. Specifically, invasively measured ascending aortic pressure pulses ("AA") and invasively and non-invasively measured carotid artery ("CA"), brachial artery ("BA") and radial artery ("RA") pressure pulses are accumulated.

Next, the processor 58 derives for each individual the Fourier transforms of the various aortic and peripheral pulse waves, and generates for each individual the transfer functions:

$$H^*(w)_{AA-BA} = BA(w)/AA(w)$$
$$H^*(w)_{AA-RA} = RA(w)/AA(w)$$
$$H^*(w)_{AA-CA} = CA(w)/AA(w)$$

where AA(w), BA(w), RA(w) and CA(w) are the Fourier transforms of the various pulses. The transfer function processor 58 then, to account for differences in heart rates between individuals, applies a smoothing function to each group of corresponding transfer functions $H^*(w)_{AA-BA}$, $H^*(w)_{AA-RA}$ and $H^*(w)_{AA-CA}$, and generates a set of generalized transfer functions, H(w). Thereafter the system uses these transfer functions, H(w), to synthesize ascending aortic pressure pulses from measured peripheral artery pressure pulses.

Figures 13A-C are graphs of a set of generalized transfer functions, H(w). Specifically, Figure 13A is a graph of $H(w)_{AA-CA}$, Figure 13B is a graph of $H(w)_{AA-BA}$ and Figure 13C is a graph of $H(w)_{AA-RA}$. Measurements were taken and separate transfer functions derived for two groups of patients, namely, a group of patients being treated with nitroglycerin (the TNG group) and a group of patients not being treated with nitroglycerin (the control group). The two sets of transfer functions were virtually identical to each other. From these results one can conclude that the depicted transfer functions are generally applicable.

Referring now to Figure 14, the pressure pulse in the ascending aorta may be synthesized from measured peripheral artery pulses using either a frequency-domain calculation method or a time-domain calculation method. Using the frequency-domain calculation method, peripheral pulse wave information, from either an invasive or a non-invasive measuring device, is applied to a Fourier transform processor 60. The processor 60 then derives the Fourier transform of the peripheral wave, for example, BA(w).

The Fourier Transform, BA(w), and the corresponding transfer function, $H(w)_{AA-BA}$, are applied to an Inverse Fourier transform processor 62, which first divides the derived Fourier

transform, BA(w), by the transfer function, producing the Fourier transform of the corresponding ascending aortic pressure pulse, AA(w). The processor 62 then calculates the inverse Fourier transform of AA(w), to obtain the time domain representation of the aortic pressure pulse, AA(t). The time domain information may be displayed graphically as shown by curve 64 in Figure 15, which is a synthesized ascending aorta pulse corresponding to the brachial artery shown, in graphic form, in Figure 16.

Referring again to the exemplary curve 64 of Figure 15, using this frequency-domain calculation method the system produces, with a lag time of approximately one heart beat, the synthesized ascending aortic pressure pulse 64 which closely resembles the actual (invasively measured) ascending aortic pressure pulse, a graph of which is shown as curve 66 in Figure 15.

Alternatively, the ascending aortic pressure pulse may be synthesized by convolving the inverse Fourier transform of the multiplicative inverse of the appropriate transfer function, for example, $H(w)_{AA-BA}$, with the time domain representation of the measured peripheral artery pressure pulse, BA(t), as shown in Figure 14. Using the time domain method of synthesizing the ascending aortic pressure pulse, the system produces the synthesized ascending aortic pressure pulse in essentially real time, that is, without a lag time of a full heart beat.

Figures 17-22 are graphs of synthesized aortic pressure pulse waves (curves 64) and corresponding actual aortic pressure pulse waves (curves 66) and the corresponding brachial artery pressure pulses.

The current invention enables a doctor to accurately determine noninvasively the maximum pressure and the contour of the pressure pulse wave in the ascending aorta. Thus a doctor

may monitor noninvasively the effects of medication, exercise, etc. on the blood pressure in the heart and treat his or her patients more effectively. The doctor may also determine from the contour of the aortic pressure pulse wave the cause of pressure problems for a particular patient.

An increase in maximum aortic pressure in a particular patient may, for example, be due to a number of causes, each of which should be treated with different medications. A doctor may learn from examining the contour of the (synthesized) aortic pressure pulse wave the cause of an increase in aortic pressure and/or the effects of a particular medication administered to the patient.

Before the current invention a doctor could not easily and/or quickly determine the causes of increased aortic pressure in traumatized patients, such as, patients in shock, who require immediate attention. Accordingly, the doctor could not gauge the appropriateness of medication or other treatment. Using the current invention the doctor may easily and quickly examine the contour of the ascending aortic pressure pulse wave and may thus readily determine probable causes, or eliminate possible causes, for the increase in aortic pressure and/or monitor the patient's response to medication. The doctor may thus avoid traumatizing the patient further by administering to him or her a medication which is ineffective in treating the cause of the increased aortic pressure or, even worse, by administering a medication which exacerbates the condition by causing a further increase in the pressure.

The foregoing description has been limited to a number of specific embodiments of this invention. It will be apparent, however, that variations and modifications may be made to the invention, with the attainment of some or all of the advantages of the invention. Therefore, it is the object of the appended claims to cover all such variations and

modifications as come within the true spirit and scope of the invention.

CLAIMS

1. A method of synthesizing the contour of an aortic pressure pulse, said method comprising the steps of:

A. measuring pressure pulses in a peripheral artery;

B. deriving a Fourier transform for the measured peripheral pulses;

C. dividing the peripheral pulse Fourier transform by a transfer function H(w) relating a Fourier transform of pressure pulses in the peripheral artery and a Fourier transform of pressure pulses in the aorta, thereby producing a Fourier transform associated with the aortic pressure pulse; and

D. deriving the inverse of the Fourier transform associated with the aortic pressure pulse, thereby producing a time-domain representation of an ascending aortic pressure pulse.

2. The method of claim 1, wherein the peripheral artery from which measurements are taken is an upper body peripheral artery.

3. The method of claim 2, wherein said method includes the step of presenting graphically the time-domain representation of the aortic pressure pulse.

4. A method of synthesizing the contour of an aortic pressure pulse, said method comprising the steps of:

A. measuring pressure pulses in a peripheral artery and deriving a peripheral pulse function;

B. convolving the peripheral pulse function with a transfer function which relates pressure pulses in the peripheral artery to pressure pulses in the

ascending aorta, thereby producing a time-domain representation of the ascending aorta pressure pulse.

5. The method of claim 4, wherein the peripheral artery from which measurements are taken is an upper body peripheral artery.

6. The method of claim 5, wherein said method includes the step of presenting a graphically the time-domain representation of the aortic pressure pulse.

7. A method of deriving generalized transfer functions relating an ascending aorta pressure pulse and a peripheral artery pressure pulse, said method comprising:

A. accumulating for a number of individuals data relating to invasively recorded ascending aorta pressure pulse contours;

B. accumulating for a number of individuals data relating to measured peripheral artery pressure pulse contours, namely, brachial, radial and carotid artery pressure pulse contours;

C. deriving for each individual Fourier transforms of the ascending aorta, brachial, radial and carotid pressure pulse contours;

D. generating for each individual transfer functions, $H^*(w)$, relating ascending aorta and peripheral artery pressure pulses:

$$H^*(w)_{AA-BA} = BA(w)/AA(w)$$
$$H^*(w)_{AA-RA} = RA(w)/AA(w)$$
$$H^*(w)_{AA-CA} = CA(w)/AA(w)$$

E. grouping the transfer functions of all the individuals into groups corresponding to each of the peripheral arteries, namely, $H^*(w)_{AA-BA}$, $H^*(w)_{AA-RA}$ and $H^*(w)_{AA-CA}$ groups and applying to each group a smoothing function, which reduces differences between the individual transfer functions attributable to differences in heart rates between individuals, to generate generalized transfer functions:

8. The method of deriving generalized transfer functions of claim 7, wherein said step of accumulating data relating to measured peripheral artery pressure pulse contours includes accumulating data from invasively measured peripheral pressure pulses.

9. The method of deriving generalized transfer functions of claim 7, wherein said step of accumulating data relating to measured peripheral artery pressure pulse contours includes accumulating data from non-invasively measured peripheral pressure pulses.

10. The method of deriving generalized transfer functions of claim 9, wherein said step of accumulating data relating to measured peripheral artery pressure pulse contours further includes accumulating data from invasively measured peripheral pressure pulses.

11. A method of deriving a generalized transfer function relating an ascending aorta pressure pulse and a radial artery pressure pulse, said method comprising:

A. accumulating for a number of individuals data relating to invasively recorded ascending aorta

pressure pulse contours;

B. accumulating for a number of individuals data relating to measured radial artery pressure pulse contours;

C. deriving for each individual Fourier transforms of the ascending aorta and radial pressure pulse contours;

D. generating for each individual transfer functions, $H^*(w)$, relating ascending aorta and radial artery pressure pulses:

$$H^*(w)_{AA-RA} = RA(w)/AA(w)$$

E. applying to all of said individual transfer functions a smoothing function, which reduces differences between the individual transfer functions attributable to differences in heart rates between individuals, to generate a generalized transfer function:

$$H(w)_{AA-RA} = RA(w)/AA(w).$$

12. The method of deriving a generalized transfer function of claim 11, wherein said step of accumulating data relating to measured radial artery pressure pulse contours includes accumulating data from invasively measured radial pressure pulses.

13. The method of deriving a generalized transfer function of claim 11, wherein said step of accumulating data relating to measured radial artery pressure pulse contours includes accumulating data from non-invasively measured radial pressure pulses.

14. The method of deriving a generalized transfer function of claim 13, wherein said step of accumulating data relating to measured radial artery pressure pulse contours further includes accumulating data from invasively measured radial pressure pulses.

15. A method of deriving a generalized transfer function relating an ascending aorta pressure pulse and a brachial artery pressure pulse, said method comprising:

A. accumulating for a number of individuals data relating to invasively recorded ascending aorta pressure pulse contours;

B. accumulating for a number of individuals data relating to measured brachial artery pressure pulse contours;

C. deriving for each individual Fourier transforms of the ascending aorta and brachial pressure pulse contours;

D. generating for each individual transfer functions, $H^*(w)$, relating ascending aorta and brachial artery pressure pulses:

$$H^*(w)_{AA-BA} = BA(w)/AA(w)$$

E. applying to all of said individual transfer functions a smoothing function, which reduces differences between the individual transfer functions attributable to differences in heart rates between individuals, to generate a generalized transfer function:

$$H(w)_{AA-BA} = BA(w)/AA(w).$$

16. The method of deriving a generalized transfer function of claim 15, wherein said step of accumulating data relating to measured brachial artery pressure pulse contours includes accumulating data from invasively measured brachial pressure pulses.

17. The method of deriving a generalized transfer function of claim 15, wherein said step of accumulating data relating to measured brachial artery pressure pulse contours includes accumulating data from non-invasively measured brachial pressure pulses.

18. The method of deriving a generalized transfer function of claim 17, wherein said step of accumulating data relating to measured brachial artery pressure pulse contours further includes accumulating data from invasively measured brachial pressure pulses.

19. A method of deriving a generalized transfer function relating an ascending aorta pressure pulse and a carotid artery pressure pulse, said method comprising:

A. accumulating for a number of individuals data relating to invasively recorded ascending aorta pressure pulse contours;

B. accumulating for a number of individuals data relating to measured carotid artery pressure pulse contours;

C. deriving for each individual Fourier transforms of the ascending aorta and carotid pressure pulse contours;

D. generating for each individual transfer functions, $H^*(w)$, relating ascending aorta and carotid artery

pressure pulses:

$$H^*(w)_{AA-CA} = CA(w)/AA(w)$$

E. applying to all of said individual transfer functions a smoothing function, which reduces differences between the individual transfer functions attributable to differences in heart rates between individuals, to generate a generalized transfer function:

$$H(w)_{AA-CA} = CA(w)/AA(w).$$

20. The method of deriving a generalized transfer function of claim 19, wherein said step of accumulating data relating to measured carotid artery pressure pulse contours includes accumulating data from invasively measured carotid pressure pulses.

21. The method of deriving a generalized transfer function of claim 19, wherein said step of accumulating data relating to measured carotid artery pressure pulse contours includes accumulating data from non-invasively measured carotid pressure pulses.

22. The method of deriving a generalized transfer function of claim 21, wherein said step of accumulating data relating to measured carotid artery pressure pulse contours further includes accumulating data from invasively measured carotid pressure pulses.

AMENDED CLAIMS
[received by the International Bureau
on 17 September 1990 (17.09.90);
new claims 23-28 added; other claims unchanged (6 pages)]

pressure pulses:

$$H^{*}(w)_{AA\text{-}CA} = CA(w)/AA(w)$$

E. applying to all of said individual transfer functions a smoothing function, which reduces differences between the individual transfer functions attributable to differences in heart rates between individuals, to generate a generalized transfer function:

$$H(w)_{AA\text{-}CA} = CA(w)/AA(w).$$

20. The method of deriving a generalized transfer function of claim 19, wherein said step of accumulating data relating to measured carotid artery pressure pulse contours includes accumulating data from invasively measured carotid pressure pulses.

21. The method of deriving a generalized transfer function of claim 19, wherein said step of accumulating data relating to measured carotid artery pressure pulse contours includes accumulating data from non-invasively measured carotid pressure pulses.

22. The method of deriving a generalized transfer function of claim 21, wherein said step of accumulating data relating to measured carotid artery pressure pulse contours further includes accumulating data from invasively measured carotid pressure pulses.

23. A method of determining augmentation of blood pressure in the ascending aorta, said method comprising the steps of:

A. measuring the contour of a blood pressure wave in a peripheral upper limb artery, said wave including a series of pulses with each pulse having a peak corresponding the a primary pressure wave and a peak corresponding to a secondary pressure wave;
B. determining for an average pulse the location and amplitude of the pulse peak which corresponds to the primary pressure wave;
C. determining for the average pulse the location and amplitude of a pulse peak which corresponds to the secondary pressure wave;
D. comparing the amplitudes of the primary and secondary pressure wave peaks; and
E. signaling that the blood pressure in the ascending aorta is augmented if the secondary pressure wave peak amplitude is within a predetermined range of the amplitude of the primary pressure wave peak.

24. The method of claim 23, wherein said method further includes the step of calculating an augmentation index which corresponds to the degree of augmentation of the systolic pressure by:

A. calculating a reverse shoulder index by dividing the secondary wave peak pressure above systolic onset pressure by the primary wave peak pressure above systolic onset pressure;
B. comparing the reverse shoulder index to a predetermined value;
C. signaling that the blood pressure in the ascending aorta is not augmented if the reverse shoulder index is smaller than the predetermined value; and
D. if the reverse shoulder index is larger than the predetermined value, substituting the reverse shoulder

index into the formula:

95 +0.57*index % (From the radial pulse)

where "*" represents multiplication, the numerals 95 and 0.57 are the y-intercept and slope, respectively, of a line which represents a best estimate of aortic pressure versus radial artery pressure measured invasively in a predetermined number of patients, and the sum is the augmentation index.

25. The method of claim 23, wherein said method further includes the step of calculating an augmentation index which corresponds to the degree of augmentation of the systolic pressure by:

A. calculating a reverse shoulder index by dividing the secondary wave peak pressure above systolic onset pressure by the primary wave peak pressure above systolic onset pressure;
B. comparing the reverse shoulder index to a predetermined value;
C. signaling that the blood pressure in the ascending aorta is not augmented if the reverse shoulder index is smaller than the predetermined value; and
D. if the reverse shoulder index is larger than the predetermined value, substituting the reverse shoulder index into the formula:

70 + 0.79*index % (From the brachial pulse)

where "*" represents multiplication, the numerals 70 and 0.79 are the y-intercept and slope, respectively, of a line which represents a best estimate of aortic pressure versus

brachial artery pressure measured invasively in a predetermined number of patients, and the sum is the augmentation index.

26. A method of determining systolic pressure in the ascending aorta, said method comprising the steps of:

A. measuring the contour of a systolic pressure wave in a peripheral upper limb artery, said wave including a series of pulses with each pulse having a peak corresponding the a primary pressure wave and a peak corresponding to a secondary pressure wave;

B. determining for an average pulse the amplitude of the pulse peak which corresponds to the primary pressure wave;

C. determining for the average pulse the amplitude of a pulse peak which corresponds to the secondary pressure wave;

D. calculating the maximum pressure in the ascending aorta by substituting the amplitude of the secondary pressure wave peak, P_{ss}, into the formula:

$$41.43 + 0.77*P_{ss} \text{ for radial pulse}$$

where "*" represents multiplication and the numerals 41.43 and 0.77 are the y-intercept and slope, respectively of a line which represents a best estimate of aortic systolic pressure versus radial artery second shoulder pressure, said sum being the maximum systolic pressure in the ascending aorta.

27. A method of determining systolic pressure in the ascending aorta, said method comprising the steps of:

A. measuring the contour of a systolic pressure wave in a

peripheral upper limb artery, said wave including a series of pulses with each pulse having a peak corresponding the a primary pressure wave and a peak corresponding to a secondary pressure wave;

B. determining for an average pulse the amplitude of the pulse peak which corresponds to the primary pressure wave;

C. determining for the average pulse the amplitude of a pulse peak which corresponds to the secondary pressure wave;

D. calculating the maximum pressure in the ascending aorta by substituting the amplitude of the secondary pressure wave peak, P_{ss}, into the formula:

$$28.6 + 0.82*P_{ss} \quad \text{for brachial pulse}$$

where "*" represents multiplication and the numerals 28.6 and 0.82 are the y-intercept and slope, respectively of a line which represents a best estimate of aortic systolic pressure versus brachial artery second shoulder pressure, said sum being the maximum systolic pressure in the ascending aorta.

28. The method of claim 25, wherein said method further includes the step of determining the locations of the pulse peak which corresponds to the primary pressure wave and the pulse peak which corresponds to the secondary pressure wave by:

A. determining the location and amplitude of a maximum pulse point, SMAX;

B. taking a first derivative of the pulse;

C. locating the maximum point of the first derivative;

D. taking a third derivative of the pulse;

E. determining the location of a relative maximum point of the third derivative, MAX3rd, which succeeds the maximum point of the first derivative;

F. equating the location of the primary pressure peak with the pulse point which corresponds to the MAX3rd point; and

G. if SMAX and MAX3rd occur at the same location, equating the secondary pressure peak with the first positive-to-negative zero crossing point of the third derivative which succeeds the MAX3rd point; and

H. equating the second shoulder with the SMAX point and equating the first shoulder with the MAX3rd point if SMAX and MAX3rd do not occur at the same location.

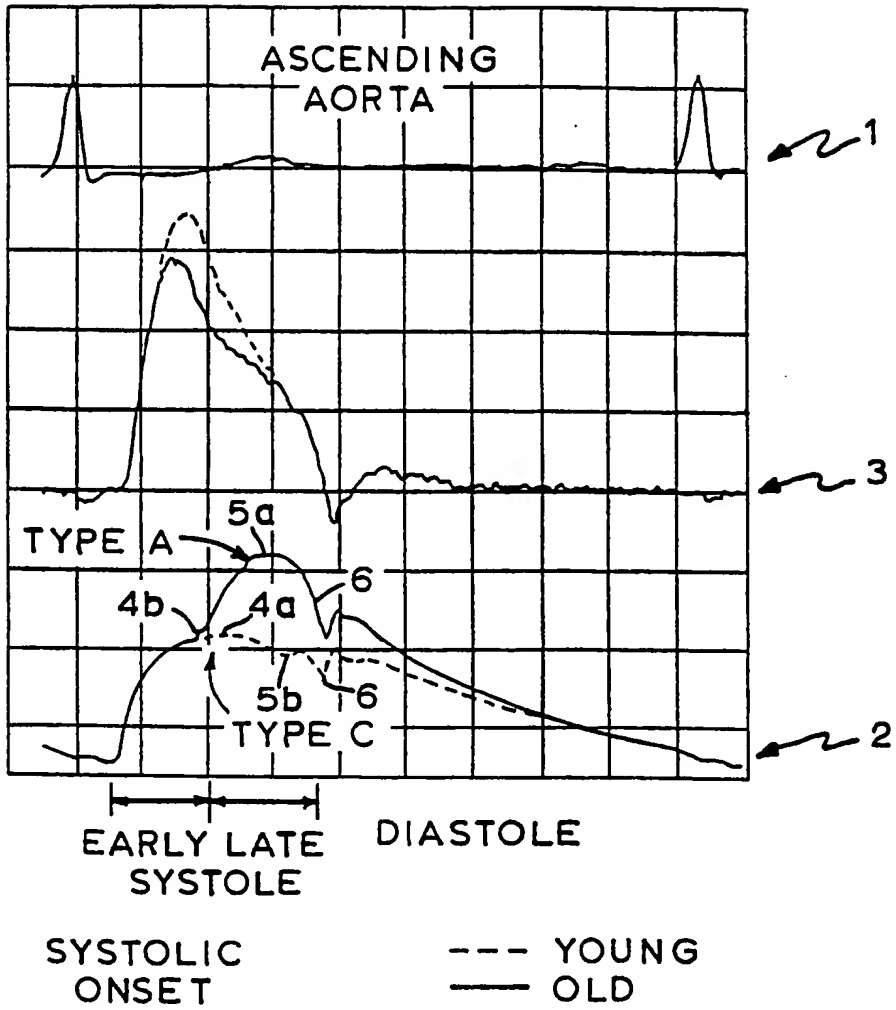

ASCENDING AORTA
1
3
2
TYPE A
5a
6
4b
4a
5b
6
TYPE C
EARLY LATE SYSTOLE
DIASTOLE
SYSTOLIC ONSET
--- YOUNG
—— OLD

FIG. 1

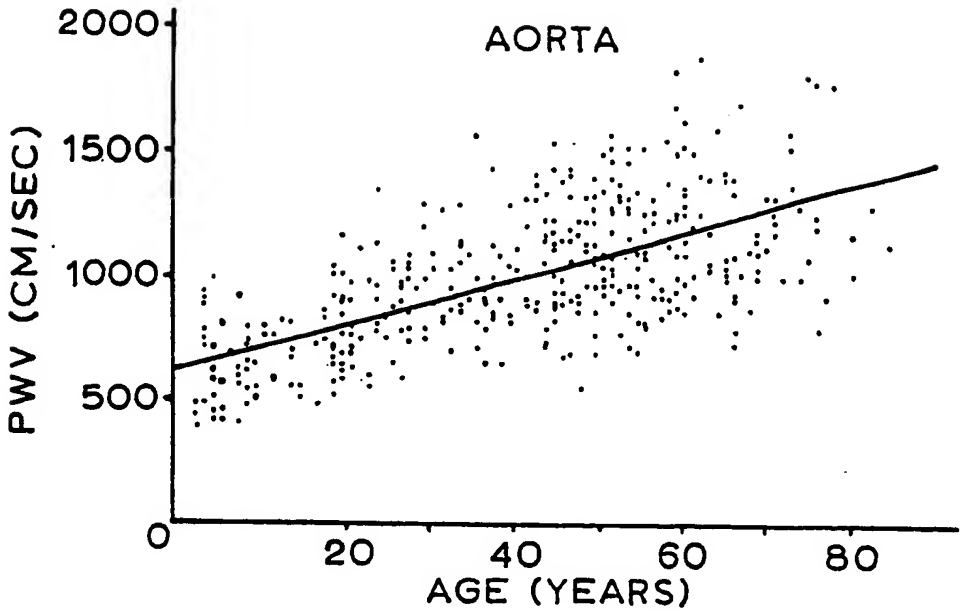


FIG. 2

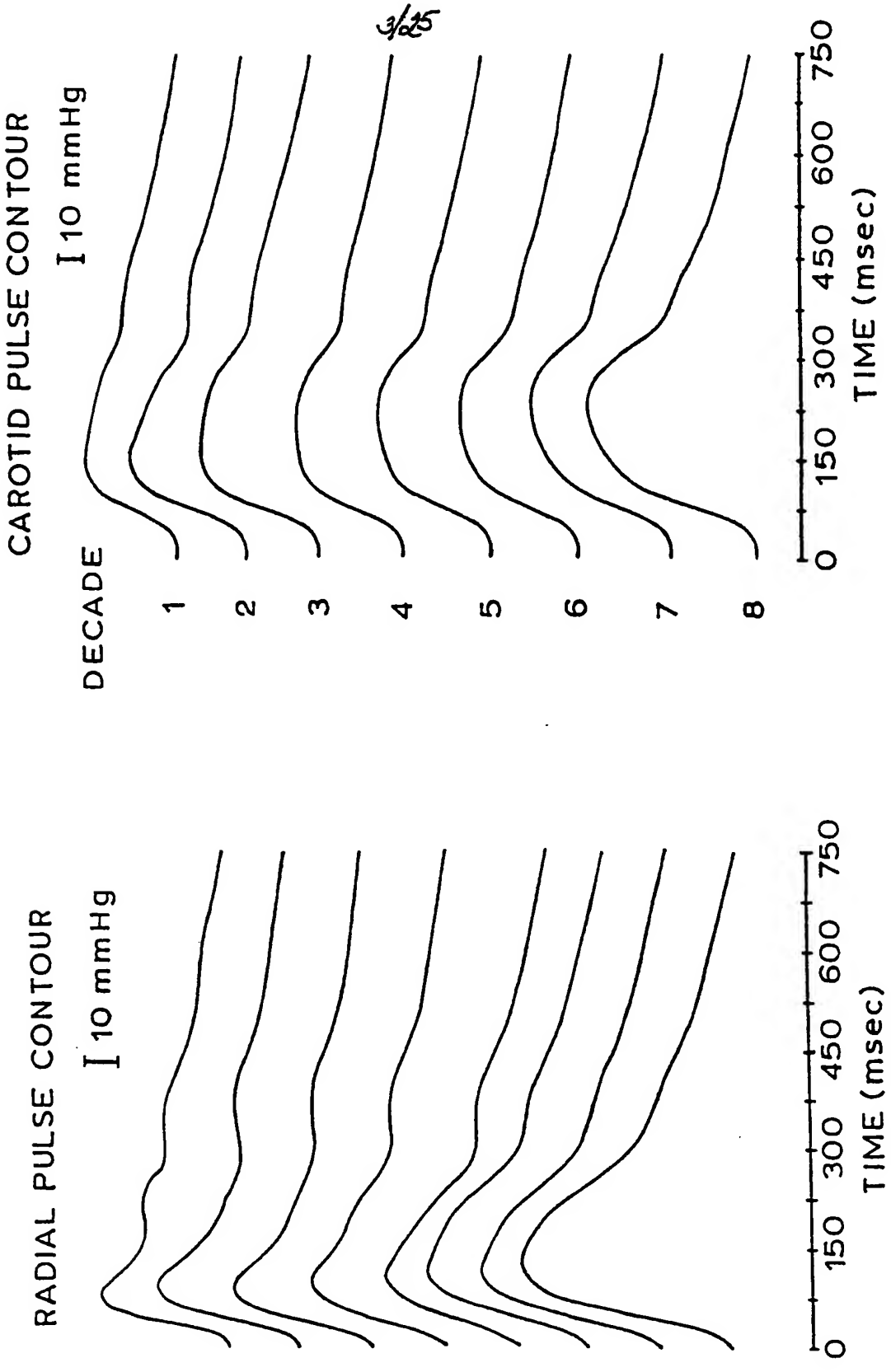

CAROTID PULSE CONTOUR
10 mmHg
DECADE
1
2
3
4
5
6
7
8
0
150
300
450
600
750
TIME (msec)
RADIAL PULSE CONTOUR
10 mmHg
0
150
300
450
600
750
TIME (msec)

FIG. 3

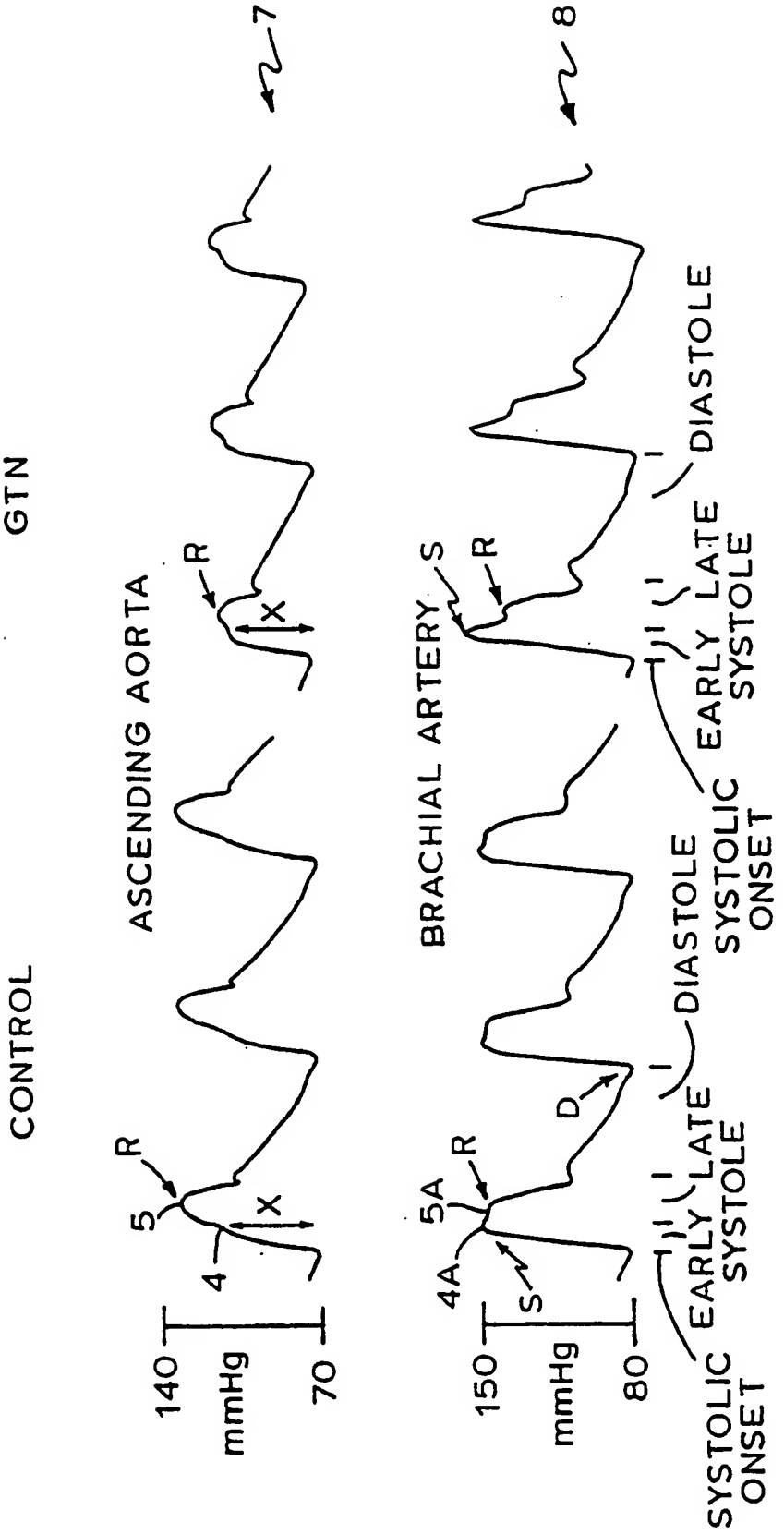

CONTROL
GTN
ASCENDING AORTA
BRACHIAL ARTERY
7
8
R
X
5
4
140
mmHg
70
S
5A
4A
D
150
80
DIASTOLE
SYSTOLIC ONSET
EARLY SYSTOLE
LATE SYSTOLE

FIG. 4

FIG. 5

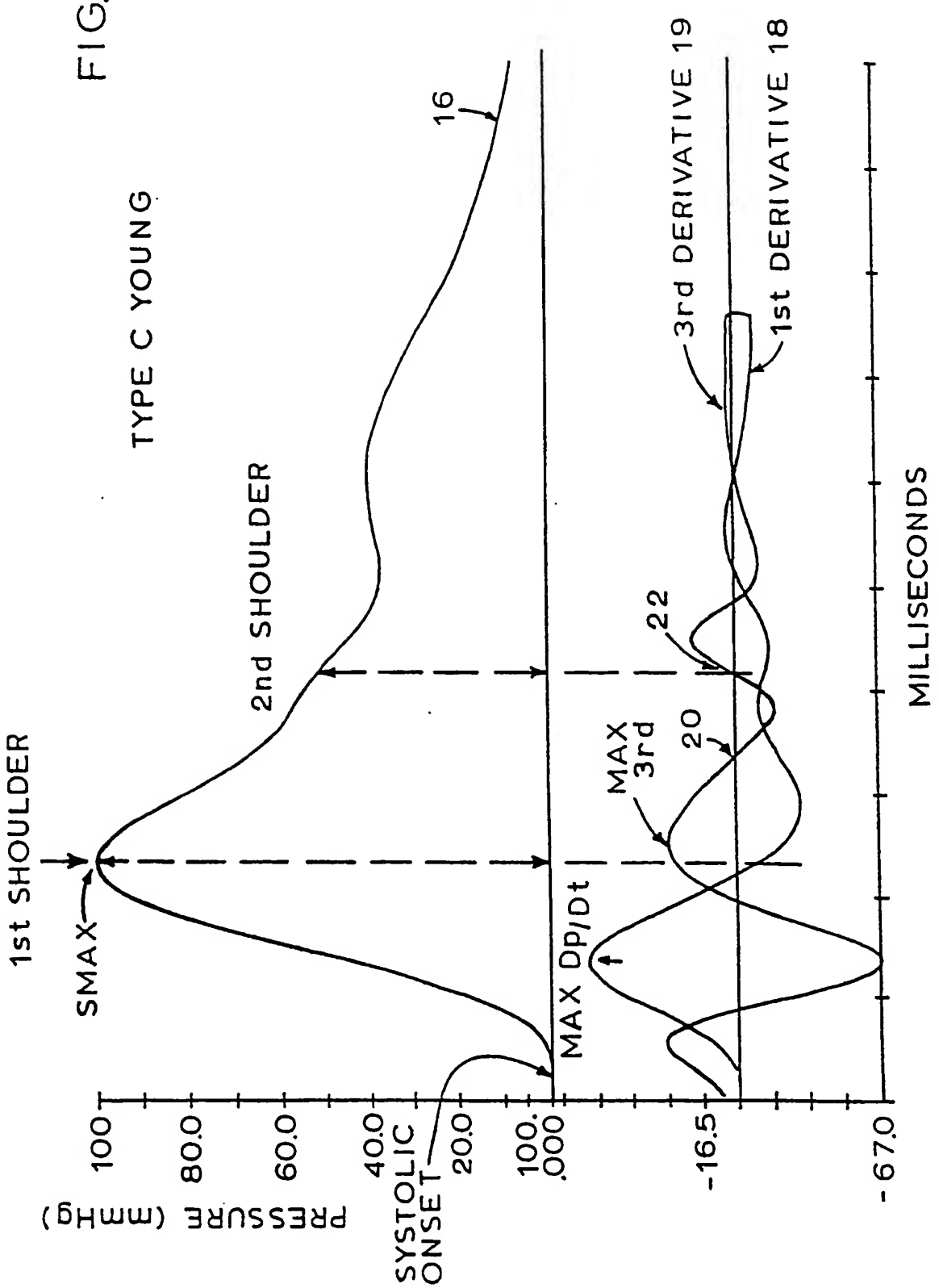

TYPE C YOUNG
1st SHOULDER
SMAX
2nd SHOULDER
16
SYSTOLIC ONSET
MAX DP/DT
MAX 3rd
20
22
3rd DERIVATIVE 19
1st DERIVATIVE 18
PRESSURE (mmHg)
100
80.0
60.0
40.0
20.0
100.000
-16.5
-67.0
MILLISECONDS

FIG. 6

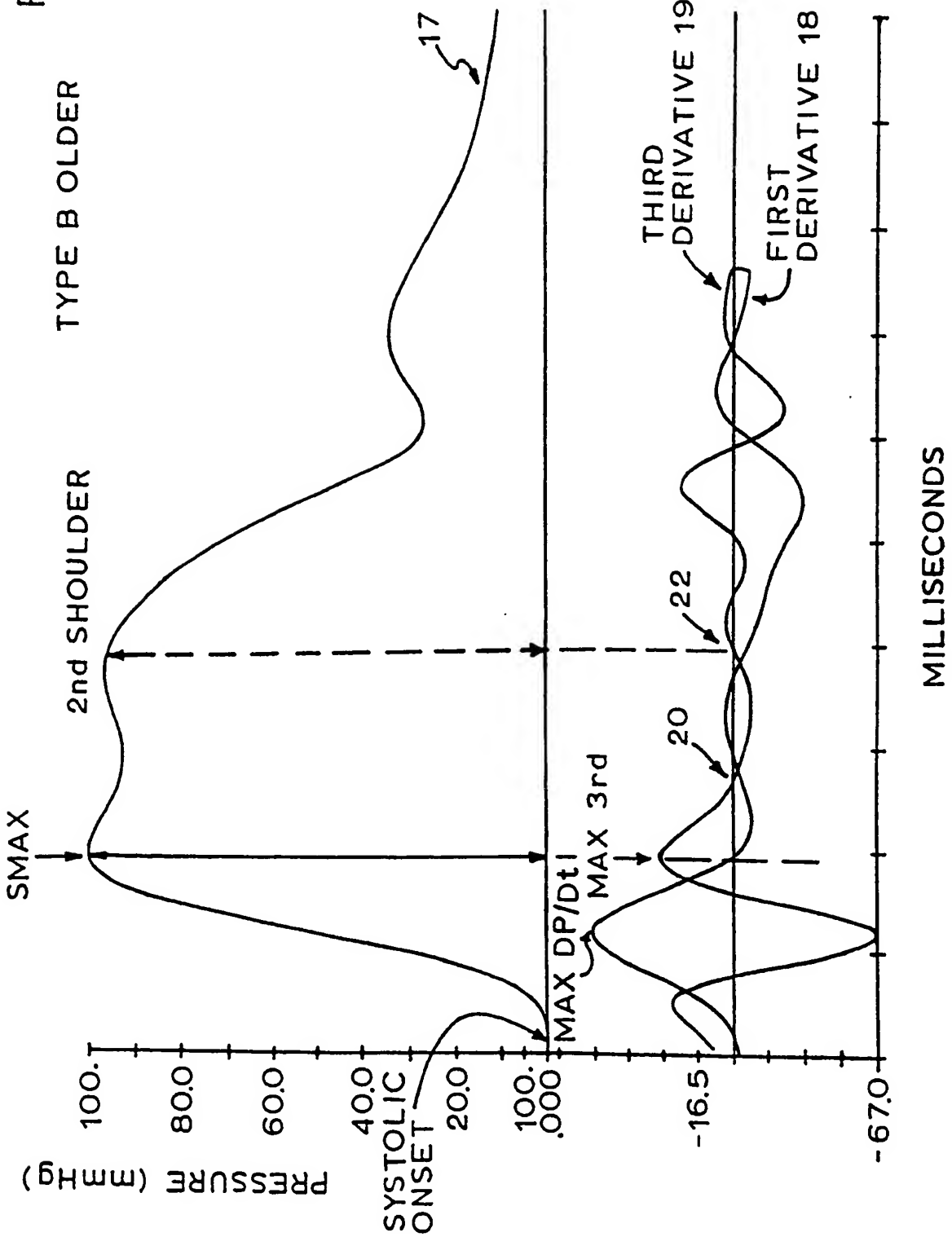
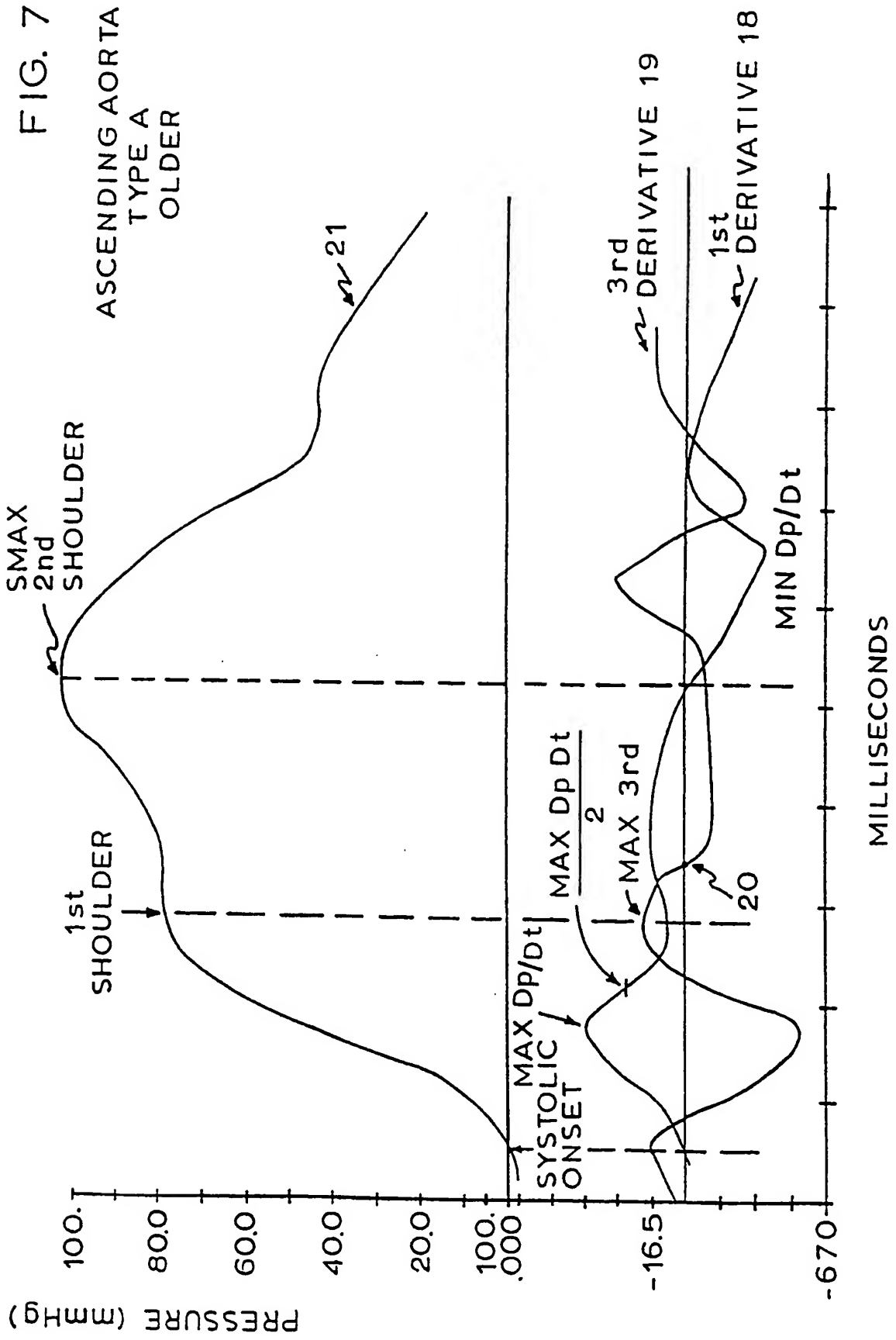

TYPE B OLDER
17
2nd SHOULDER
SMAX
22
20
MAX 3rd
MAX DP/Dt
SYSTOLIC ONSET
THIRD DERIVATIVE 19
FIRST DERIVATIVE 18
PRESSURE (mmHg)
100.
80.0
60.0
40.0
20.0
100.000
-16.5
-67.0
MILLISECONDS

FIG. 7


ASCENDING AORTA
TYPE A
OLDER
21
SMAX
2nd SHOULDER
1st
SHOULDER
3rd
DERIVATIVE 19
1st
DERIVATIVE 18
MIN Dp/Dt
MAX Dp Dt
2
MAX 3rd
20
MAX Dp/Dt
SYSTOLIC
ONSET
100.
80.0
60.0
40.0
20.0
100.
.000
-16.5
-670
PRESSURE (mmHg)
MILLISECONDS

INITIAL AND LATE PEAK FINDING FLOWCHART

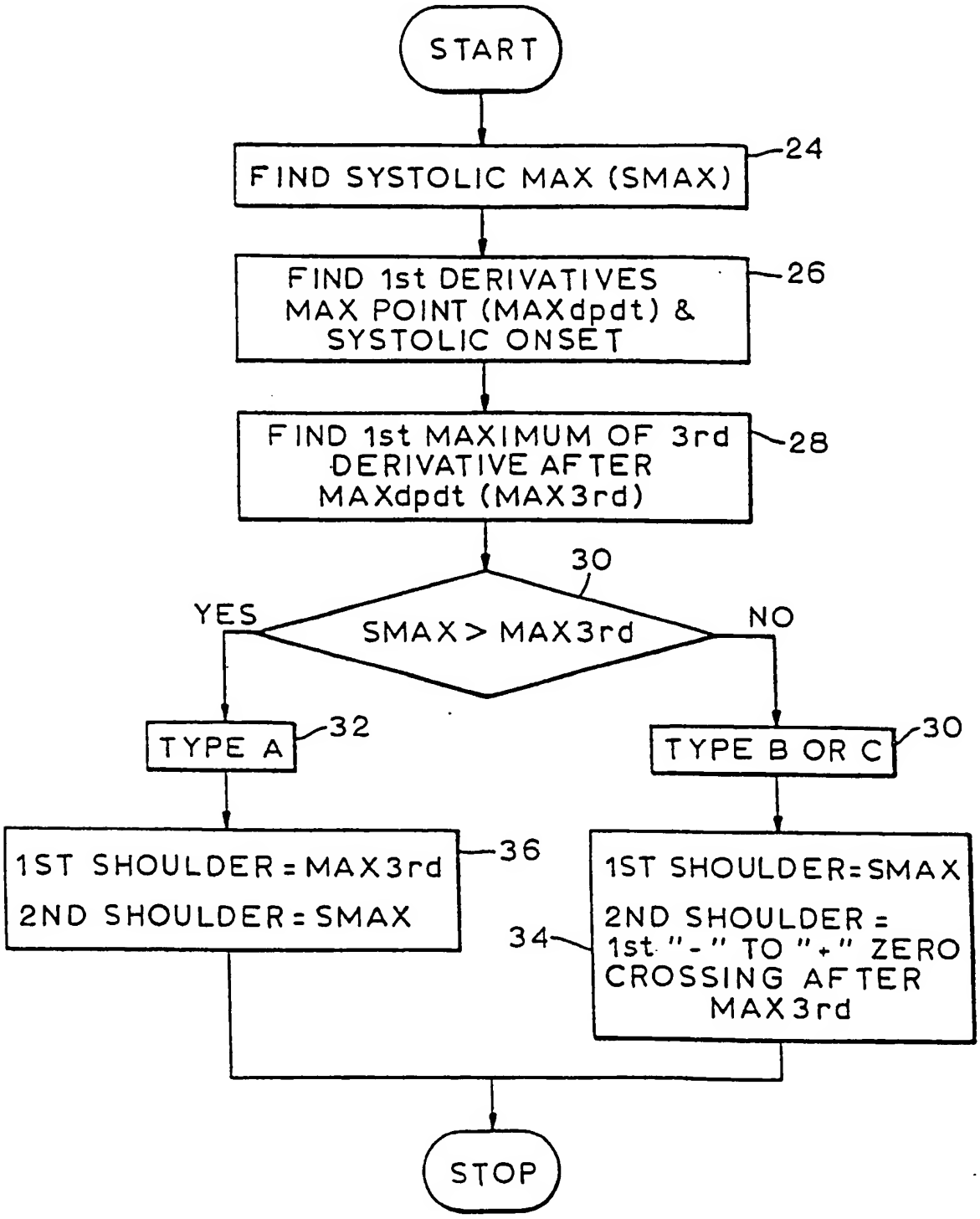


FIG. 8

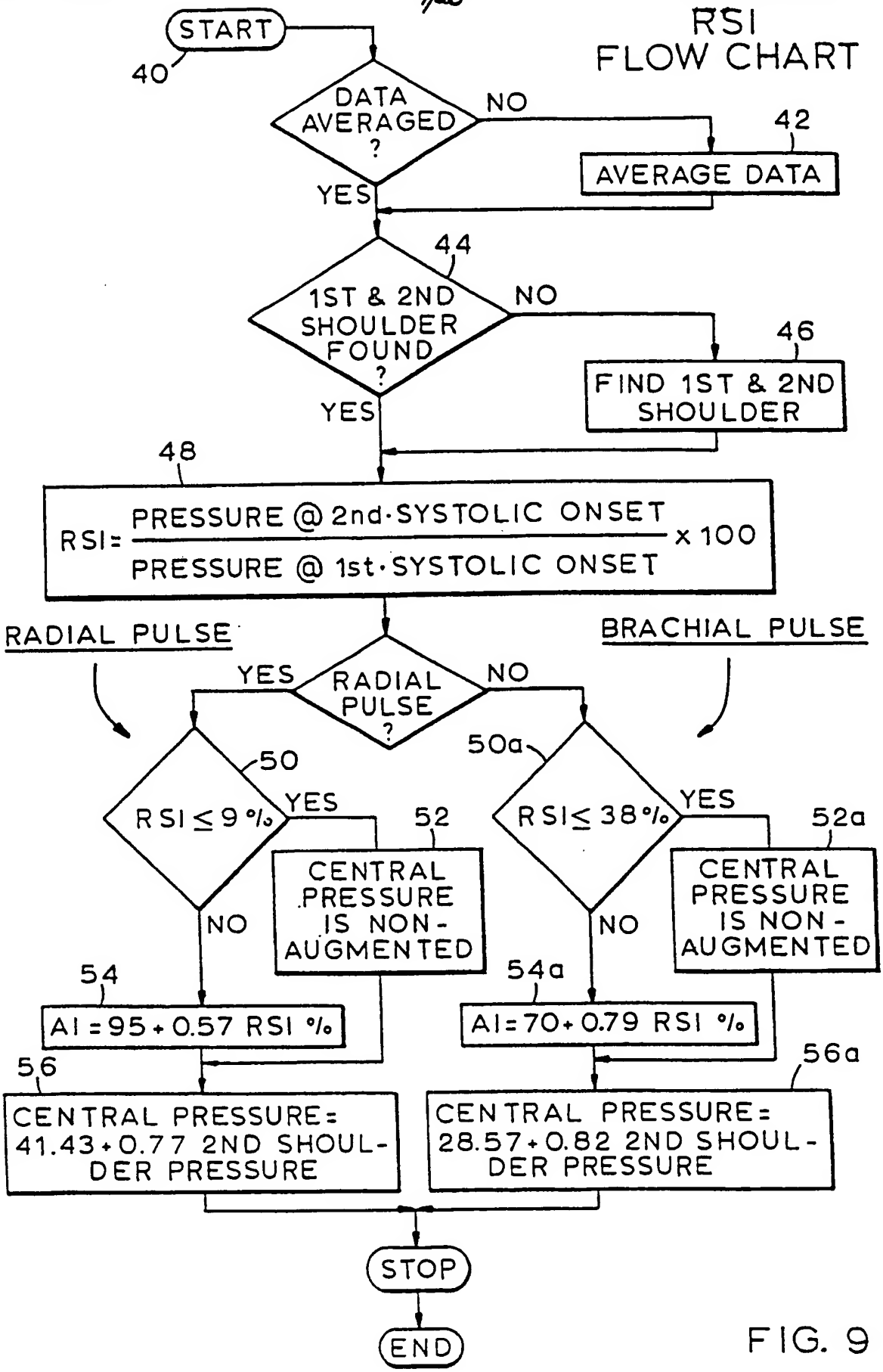

RSI
FLOW CHART
START
40
DATA AVERAGED ?
NO
42
AVERAGE DATA
YES
44
1ST & 2ND SHOULDER FOUND ?
NO
46
FIND 1ST & 2ND SHOULDER
YES
48
RSI = PRESSURE @ 2nd·SYSTOLIC ONSET / PRESSURE @ 1st·SYSTOLIC ONSET x 100
RADIAL PULSE
BRACHIAL PULSE
RADIAL PULSE ?
YES
NO
50
RSI ≤ 9 %
YES
52
CENTRAL PRESSURE IS NON-AUGMENTED
NO
54
AI = 95 + 0.57 RSI %
50a
RSI ≤ 38 %
YES
52a
CENTRAL PRESSURE IS NON-AUGMENTED
NO
54a
AI = 70 + 0.79 RSI %
56
CENTRAL PRESSURE = 41.43 + 0.77 2ND SHOULDER PRESSURE
56a
CENTRAL PRESSURE = 28.57 + 0.82 2ND SHOULDER PRESSURE
STOP
END

FIG. 9

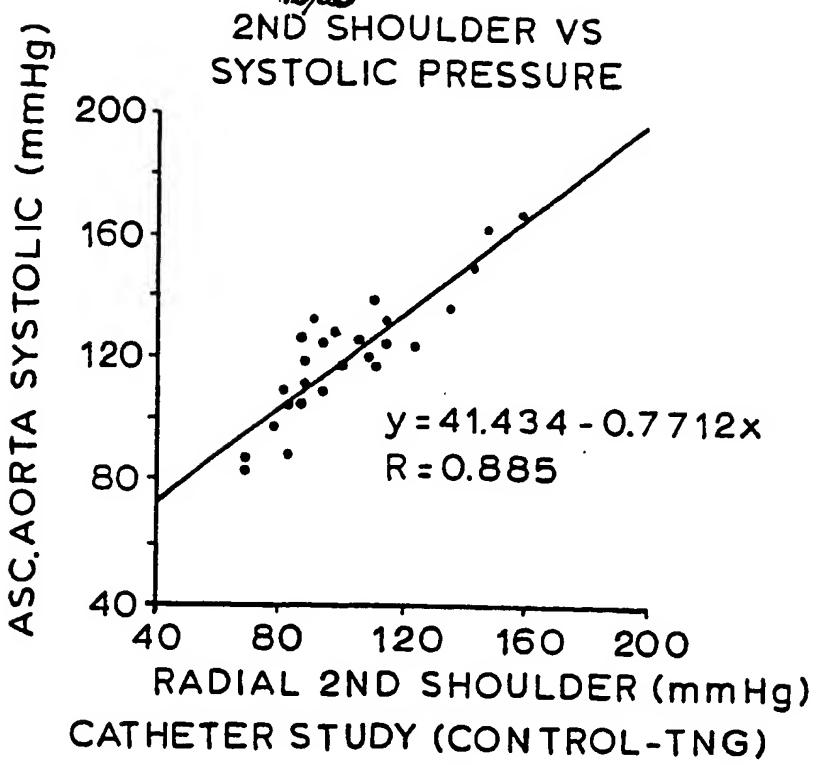


FIG. 10

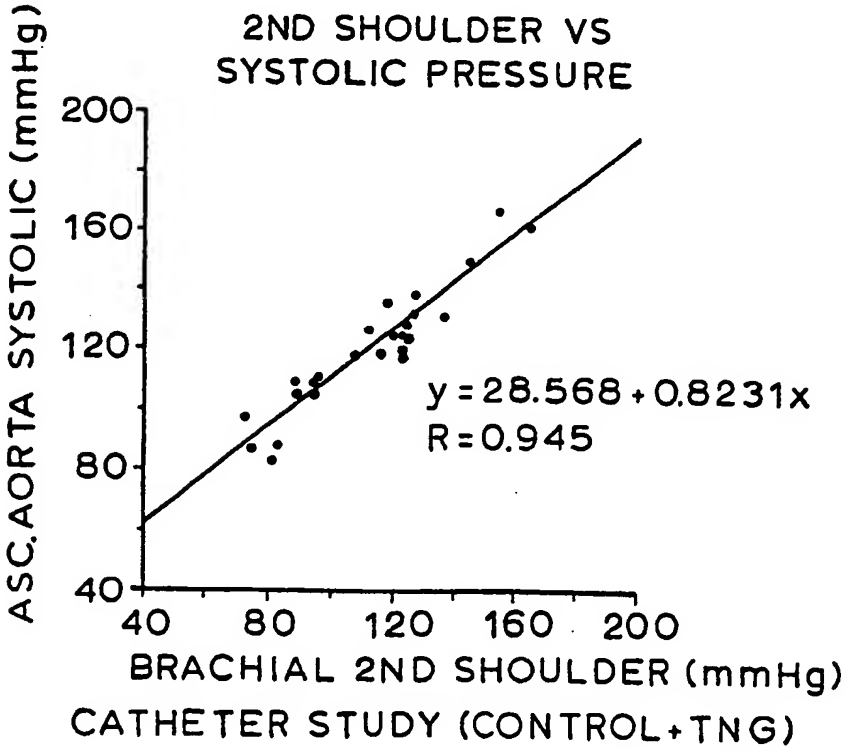


FIG. 10a

11/25

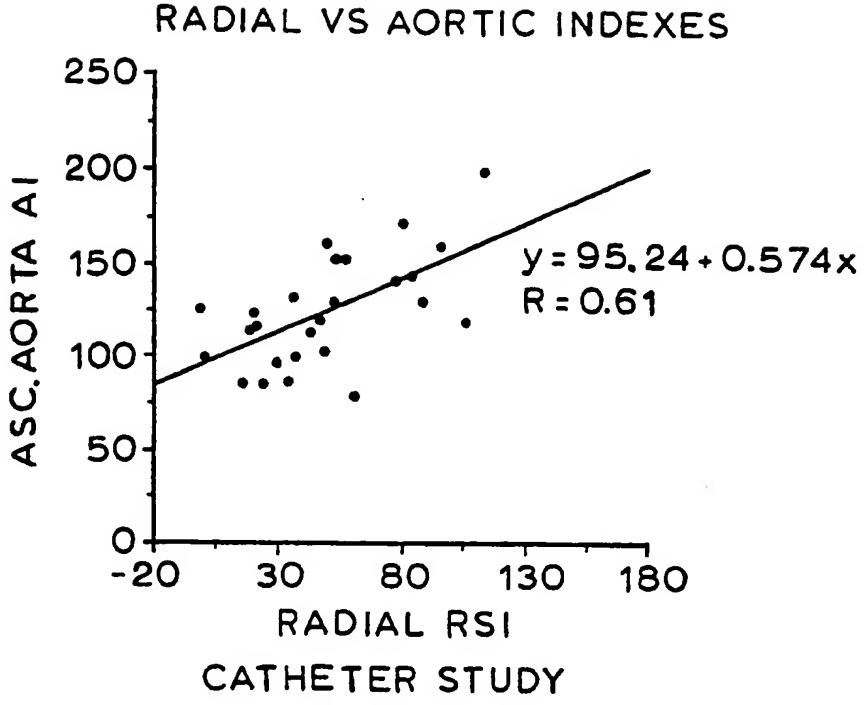

RADIAL VS AORTIC INDEXES
250
200
150
100
50
0
ASC. AORTA AI
-20
30
80
130
180
RADIAL RSI
y = 95.24 + 0.574x
R = 0.61
CATHETER STUDY

FIG. 11

12/25

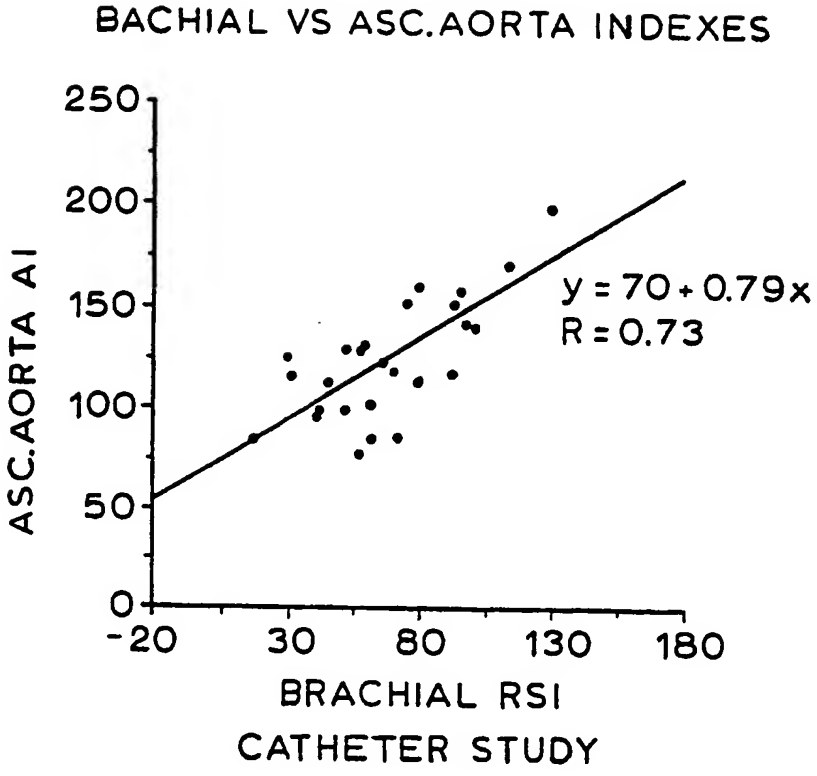

BACHIAL VS ASC.AORTA INDEXES
250
200
150
100
50
0
ASC.AORTA AI
-20
30
80
130
180
BRACHIAL RSI
CATHETER STUDY
y = 70 + 0.79x
R = 0.73

FIG. 11a

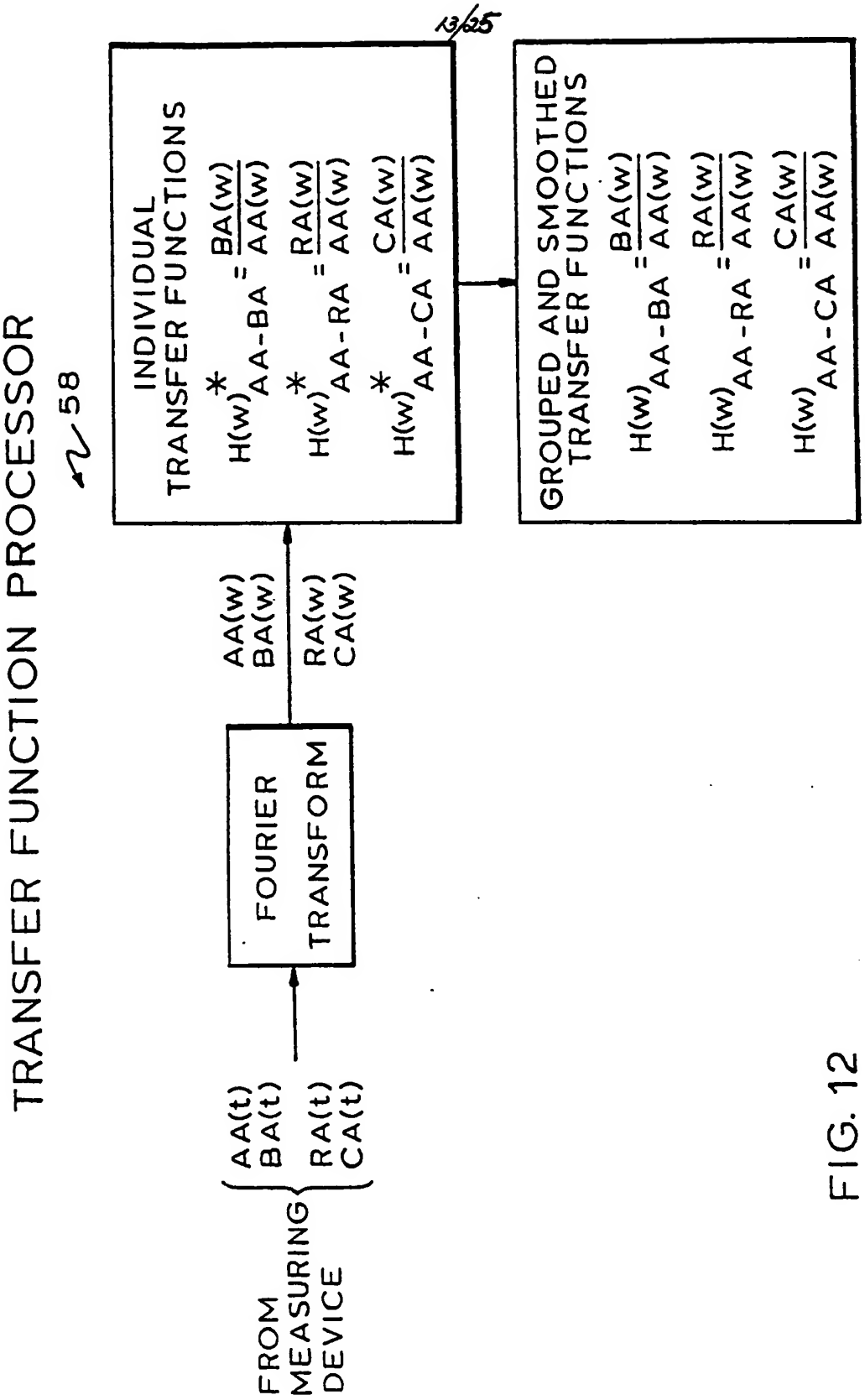

TRANSFER FUNCTION PROCESSOR
58
INDIVIDUAL TRANSFER FUNCTIONS
$H(w)_{AA-BA} = \frac{BA(w)}{AA(w)}$
$H(w)_{AA-RA} = \frac{RA(w)}{AA(w)}$
$H(w)_{AA-CA} = \frac{CA(w)}{AA(w)}$
GROUPED AND SMOOTHED TRANSFER FUNCTIONS
$H(w)_{AA-BA} = \frac{BA(w)}{AA(w)}$
$H(w)_{AA-RA} = \frac{RA(w)}{AA(w)}$
$H(w)_{AA-CA} = \frac{CA(w)}{AA(w)}$
AA(w) BA(w)
RA(w) CA(w)
FOURIER TRANSFORM
AA(t) BA(t)
RA(t) CA(t)
FROM MEASURING DEVICE

FIG. 12

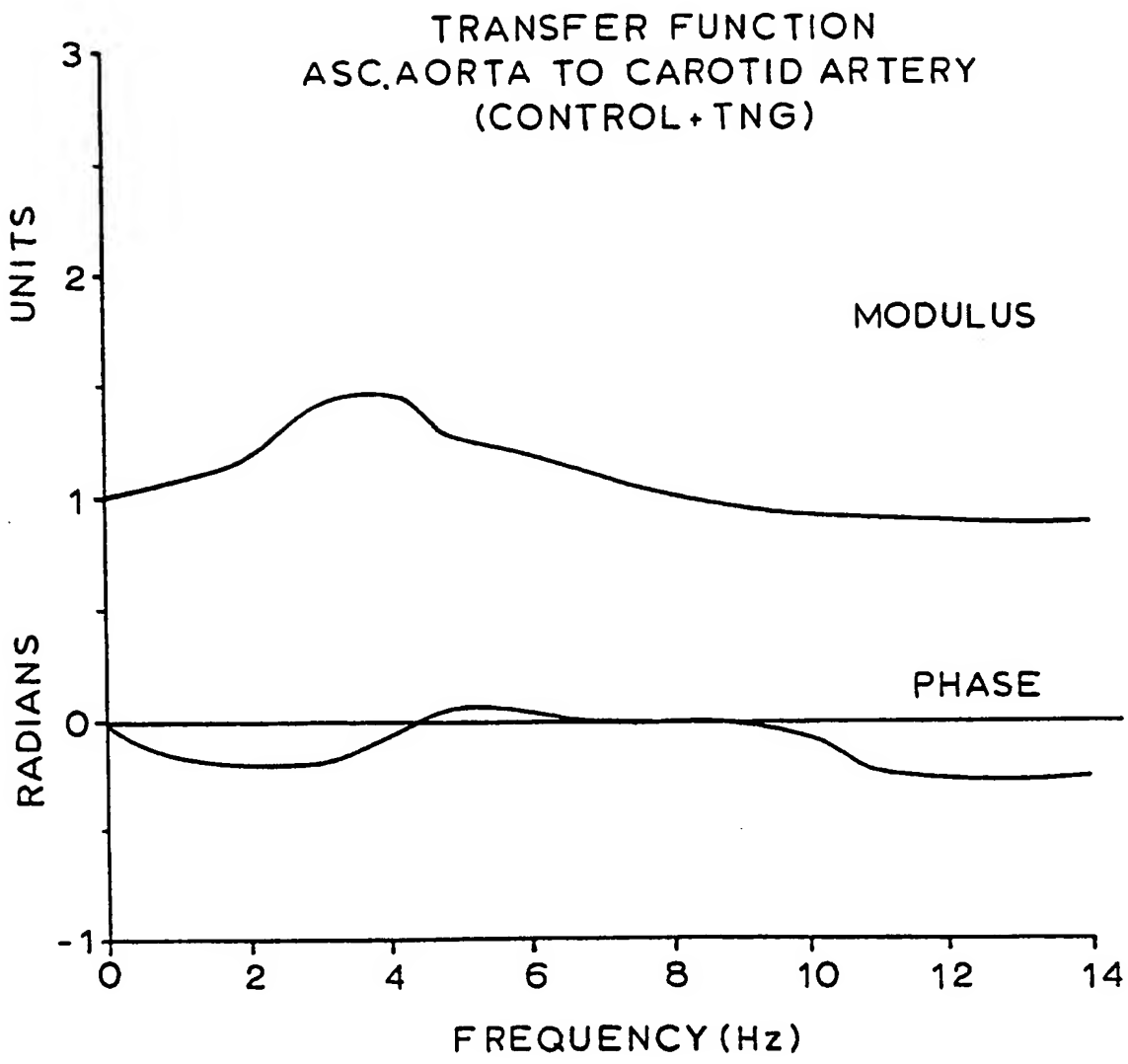

TRANSFER FUNCTION
ASC.AORTA TO CAROTID ARTERY
(CONTROL+TNG)
UNITS
RADIANS
MODULUS
PHASE
3
2
1
0
-1
0
2
4
6
8
10
12
14
FREQUENCY (Hz)

FIG. 13A

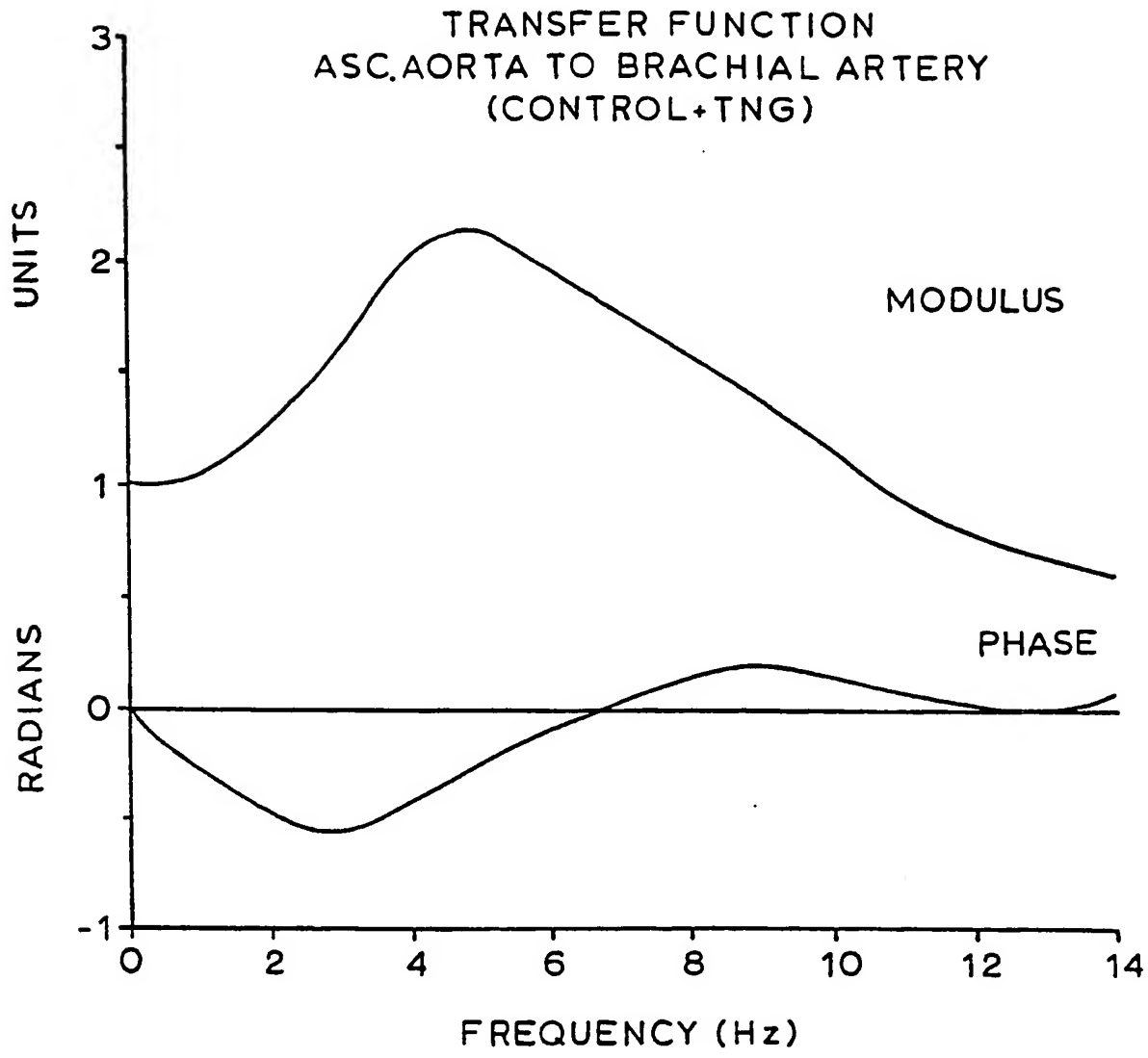

TRANSFER FUNCTION
ASC.AORTA TO BRACHIAL ARTERY
(CONTROL+TNG)
UNITS
RADIANS
MODULUS
PHASE
3
2
1
0
-1
0
2
4
6
8
10
12
14
FREQUENCY (Hz)

FIG. 13B

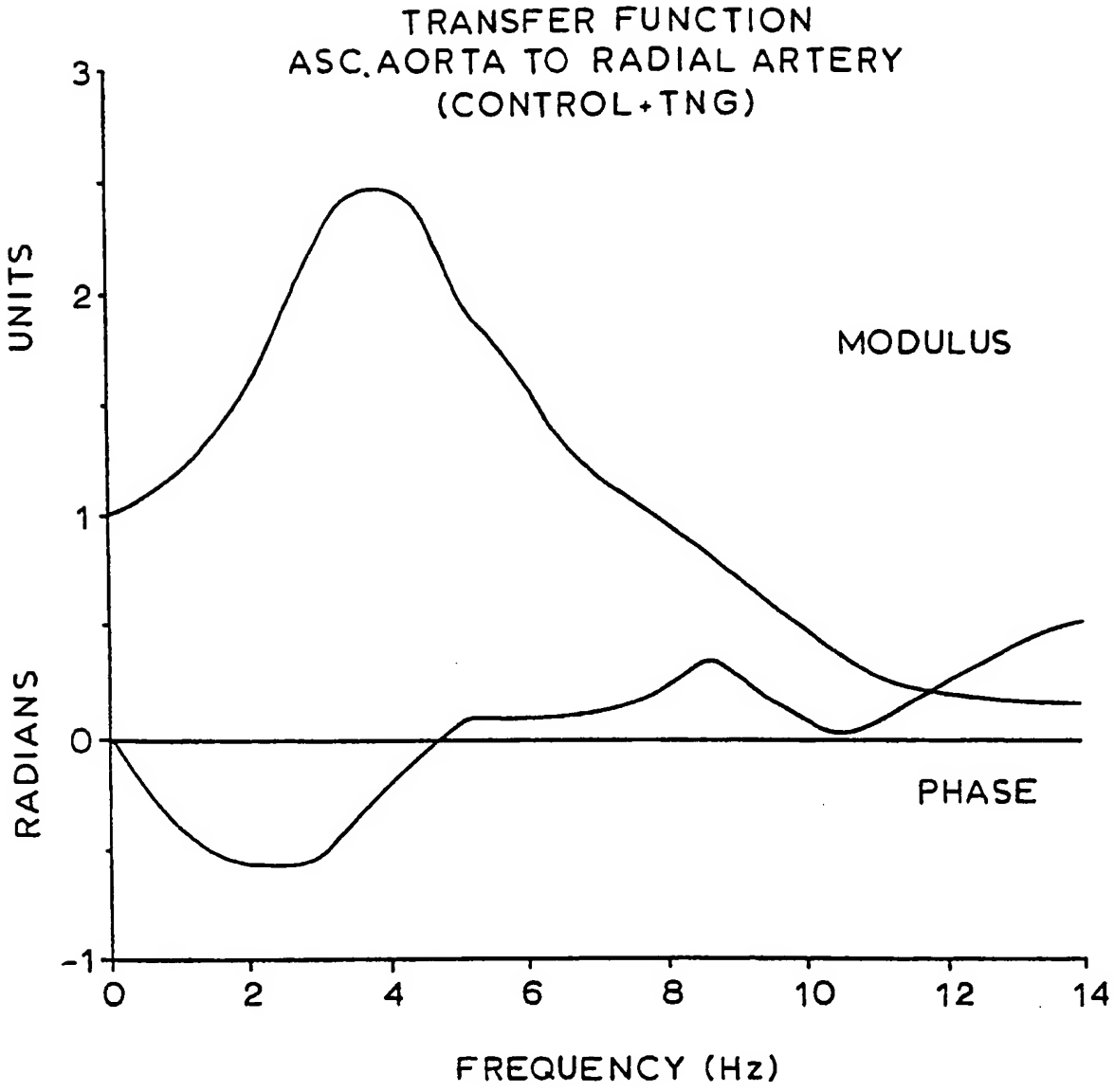

TRANSFER FUNCTION
ASC. AORTA TO RADIAL ARTERY
(CONTROL+TNG)
UNITS
RADIANS
MODULUS
PHASE
3
2
1
0
-1
0
2
4
6
8
10
12
14
FREQUENCY (Hz)

FIG. 13C

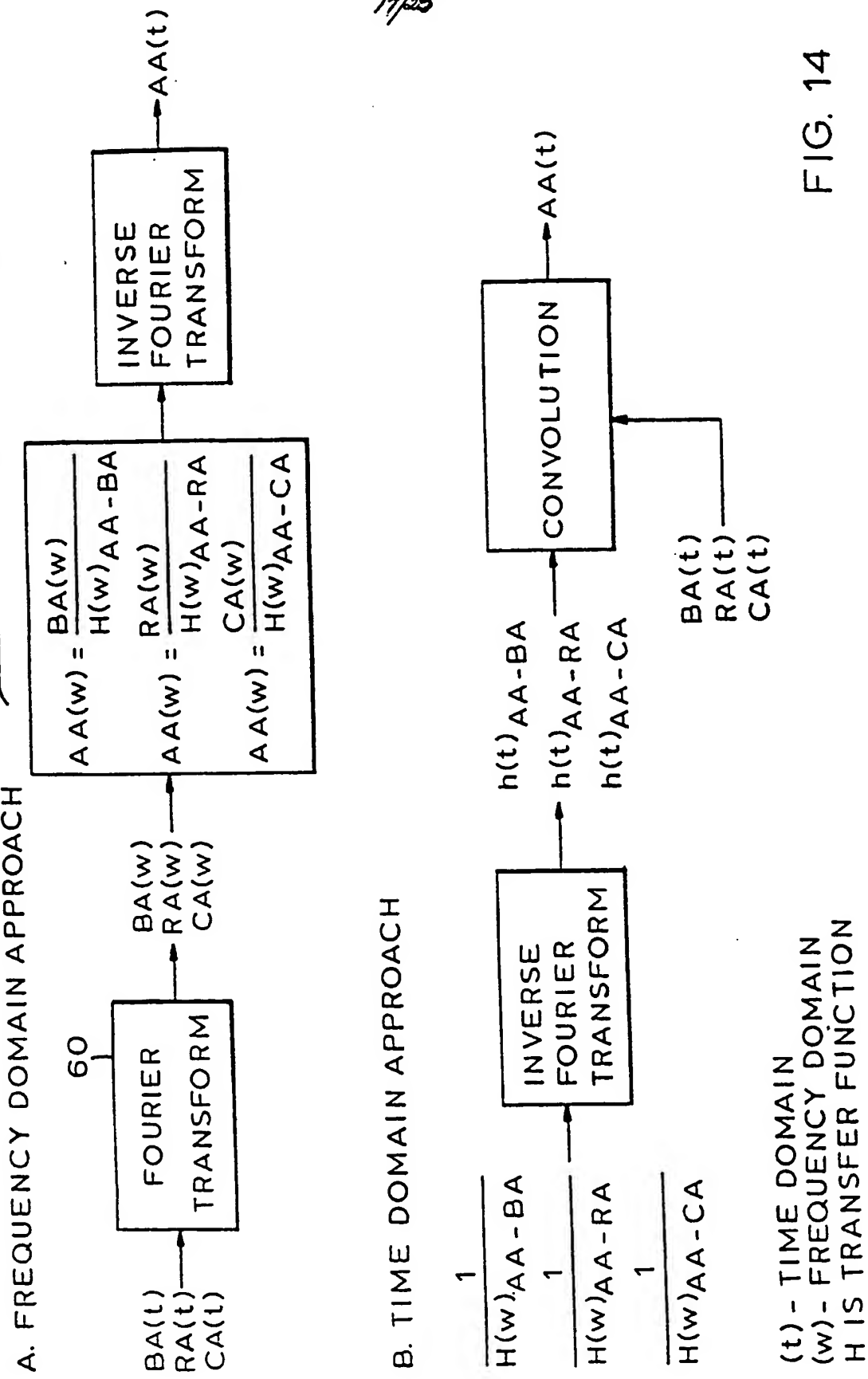

A. FREQUENCY DOMAIN APPROACH
BA(t)
RA(t)
CA(t)
60
FOURIER TRANSFORM
BA(w)
RA(w)
CA(w)
62
AA(w) = BA(w) / H(w)AA-BA
AA(w) = RA(w) / H(w)AA-RA
AA(w) = CA(w) / H(w)AA-CA
INVERSE FOURIER TRANSFORM
AA(t)
B. TIME DOMAIN APPROACH
1 / H(w)AA-BA
1 / H(w)AA-RA
1 / H(w)AA-CA
INVERSE FOURIER TRANSFORM
h(t)AA-BA
h(t)AA-RA
h(t)AA-CA
CONVOLUTION
AA(t)
BA(t)
RA(t)
CA(t)
(t) - TIME DOMAIN
(w) - FREQUENCY DOMAIN
H IS TRANSFER FUNCTION

FIG. 14

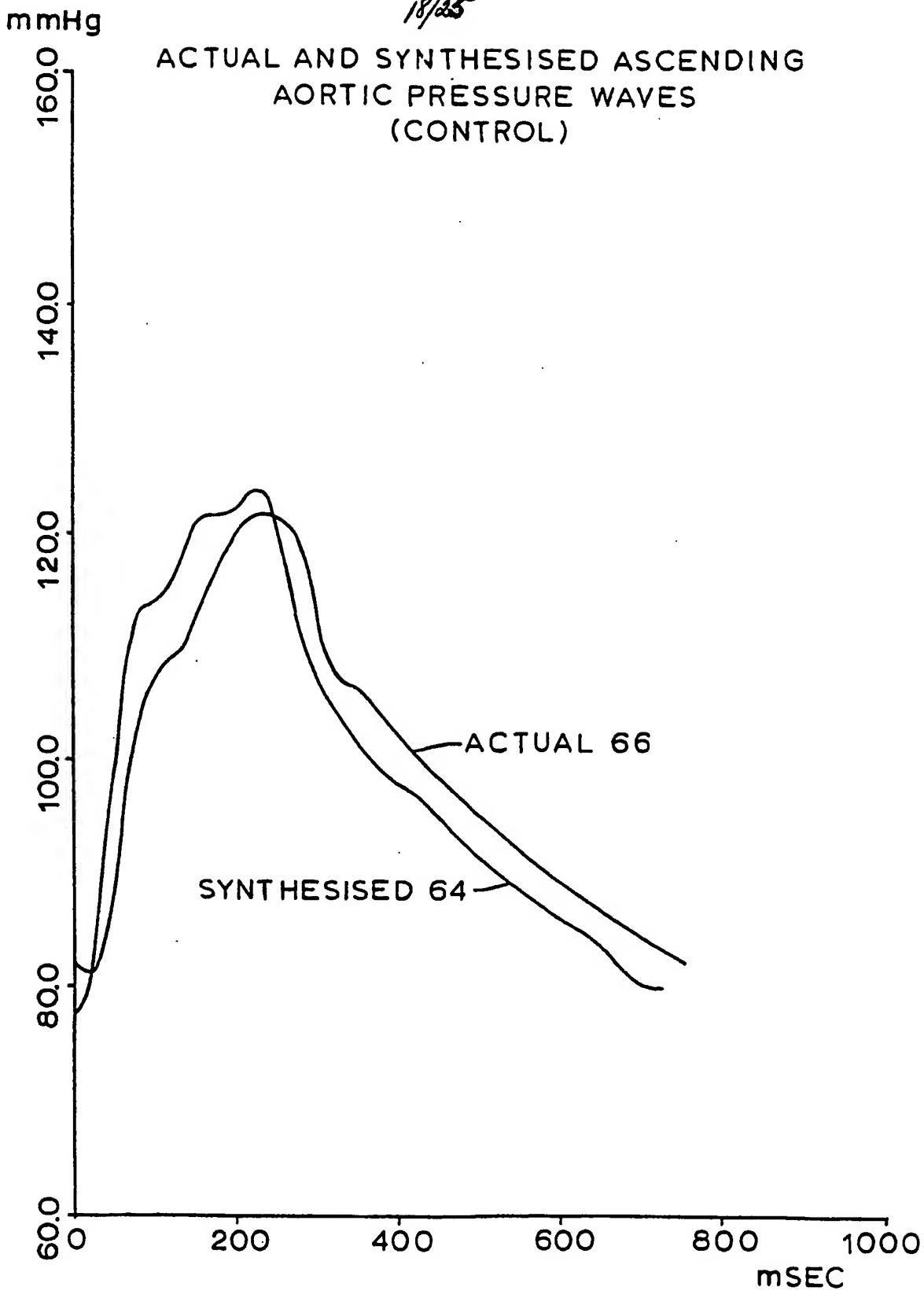

mmHg
ACTUAL AND SYNTHESISED ASCENDING
AORTIC PRESSURE WAVES
(CONTROL)
160.0
140.0
120.0
100.0
80.0
60.0
ACTUAL 66
SYNTHESISED 64
0
200
400
600
800
1000
mSEC

FIG. 15

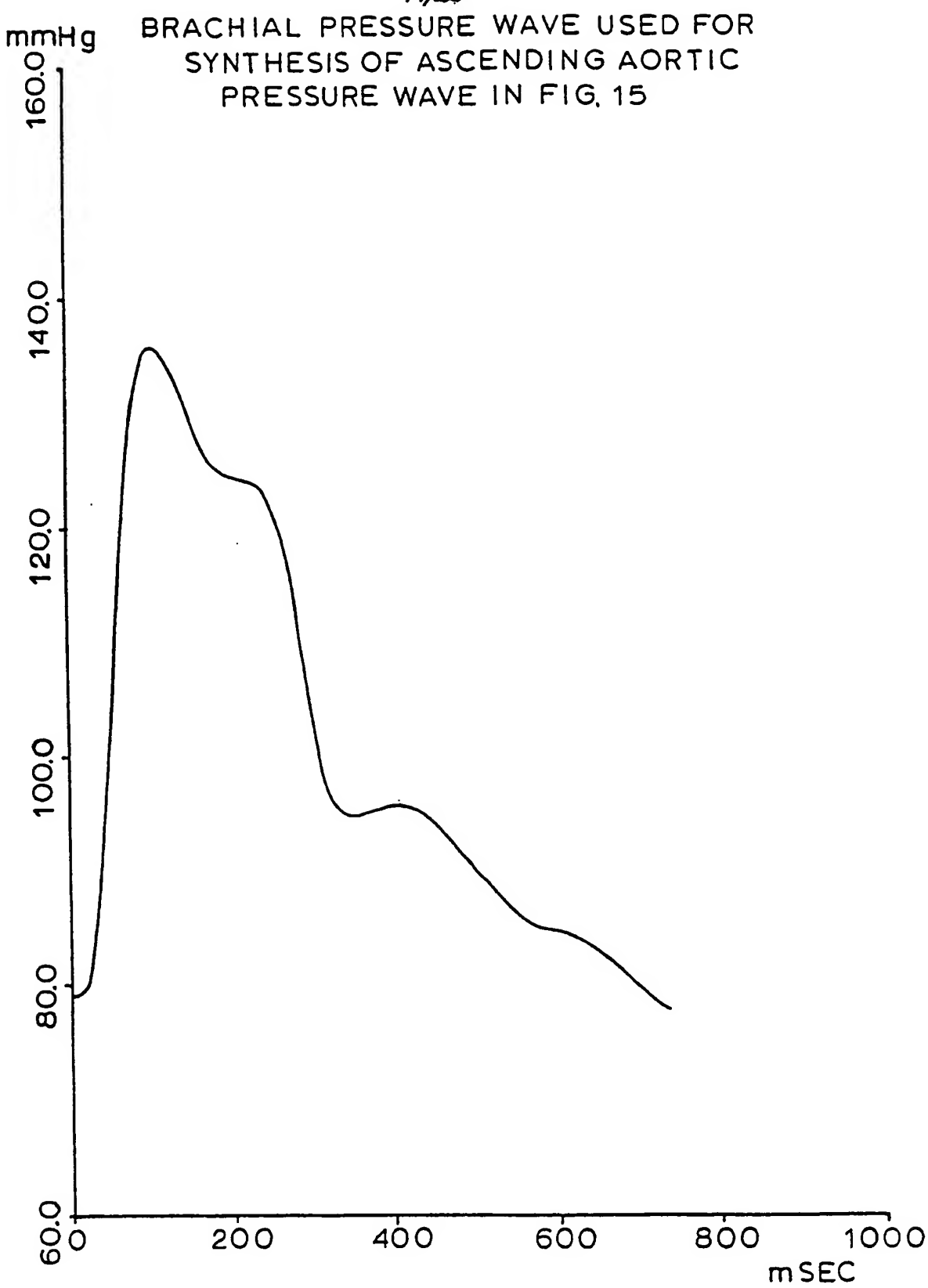

BRACHIAL PRESSURE WAVE USED FOR SYNTHESIS OF ASCENDING AORTIC PRESSURE WAVE IN FIG. 15
mmHg
160.0
140.0
120.0
100.0
80.0
60.0
0
200
400
600
800
1000
mSEC

FIG. 16

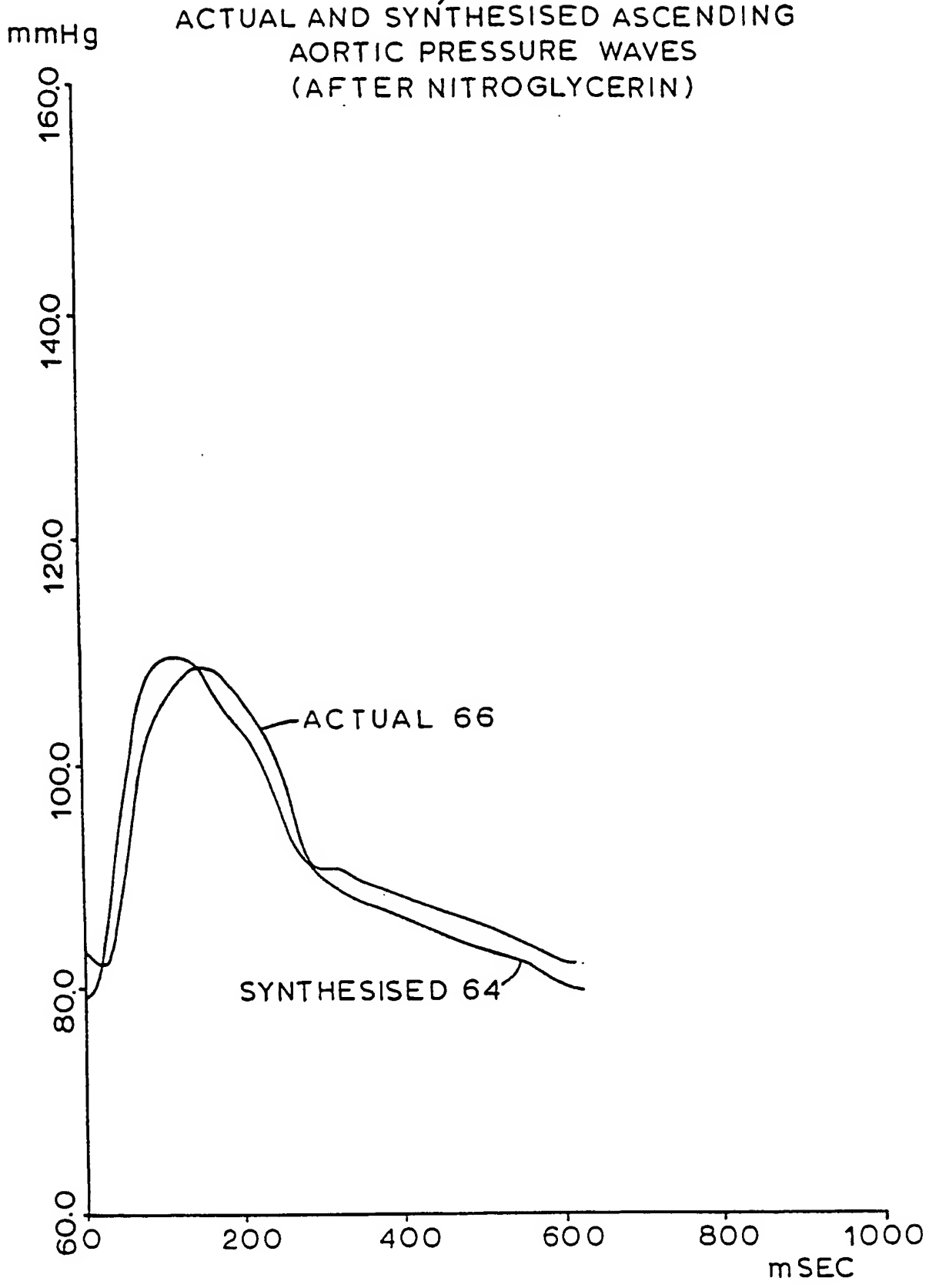

ACTUAL AND SYNTHESISED ASCENDING
AORTIC PRESSURE WAVES
(AFTER NITROGLYCERIN)
mmHg
160.0
140.0
120.0
100.0
80.0
60.0
ACTUAL 66
SYNTHESISED 64
0
200
400
600
800
1000
mSEC

FIG. 17

BRACHIAL ARTERY PRESSURE WAVE USED FOR SYNTHESIS OF ASCENDING AORTIC PRESSURE WAVE IN FIG. 17

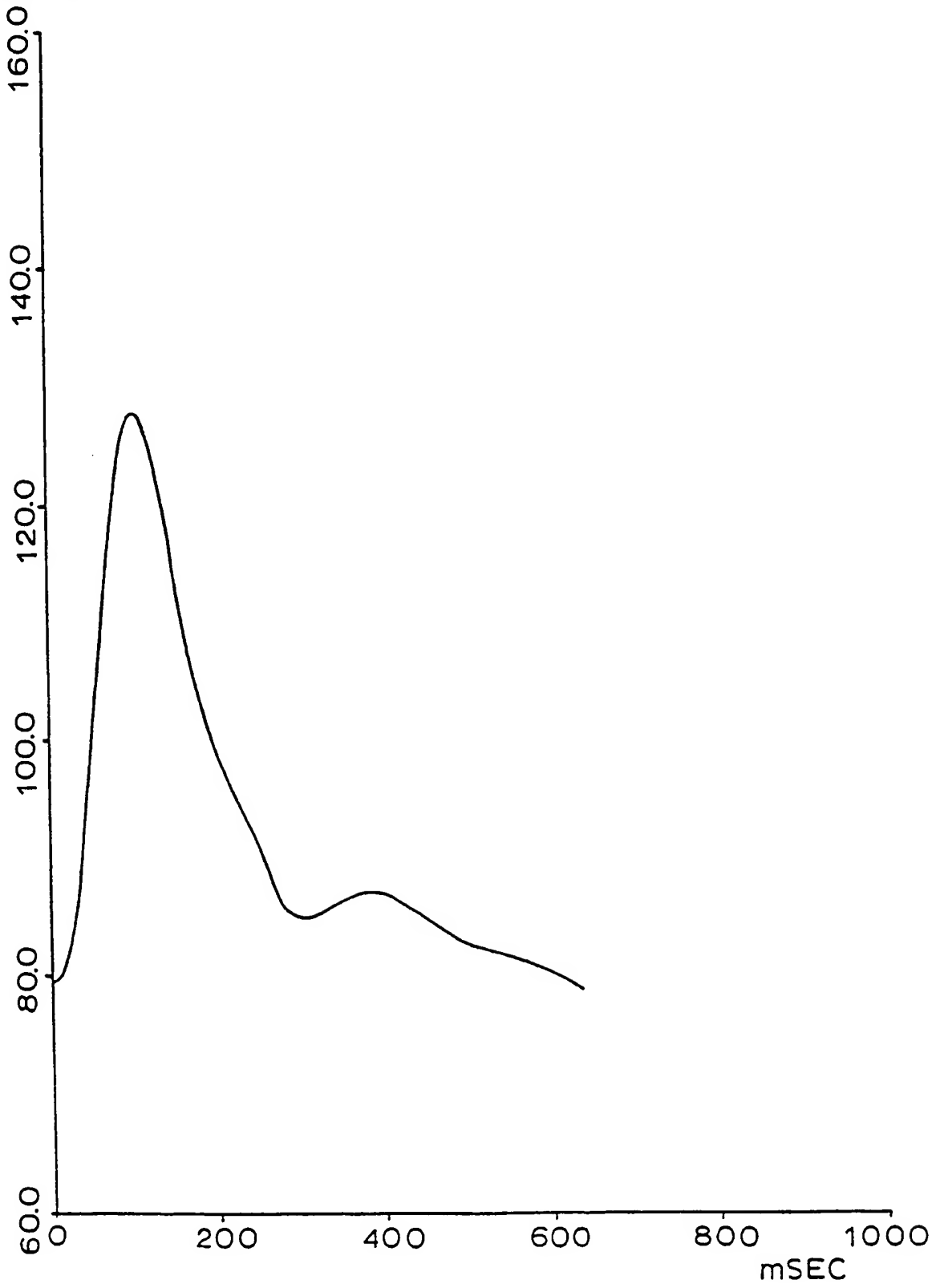


FIG. 18

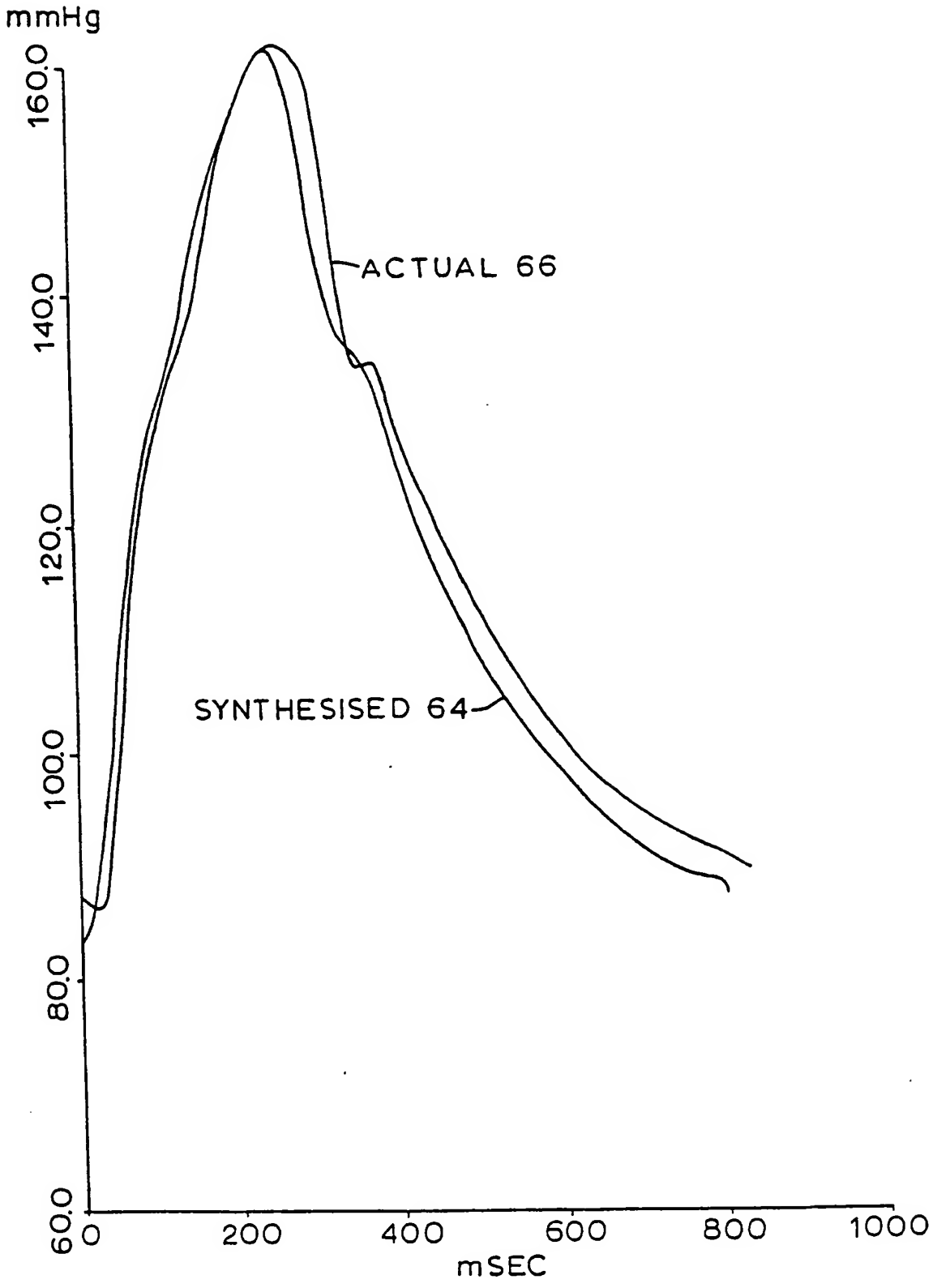

ACTUAL AND SYNTHESISED ASCENDING
AORTIC PRESSURE WAVES (CONTROL)
mmHg
160.0
140.0
120.0
100.0
80.0
60.0
ACTUAL 66
SYNTHESISED 64
0
200
400
600
800
1000
mSEC

FIG. 19

BRACHIAL ARTERY PRESSURE WAVE USED FOR SYNTHESIS OF ASCENDING AORTIC PRESSURE WAVE IN FIG. 19

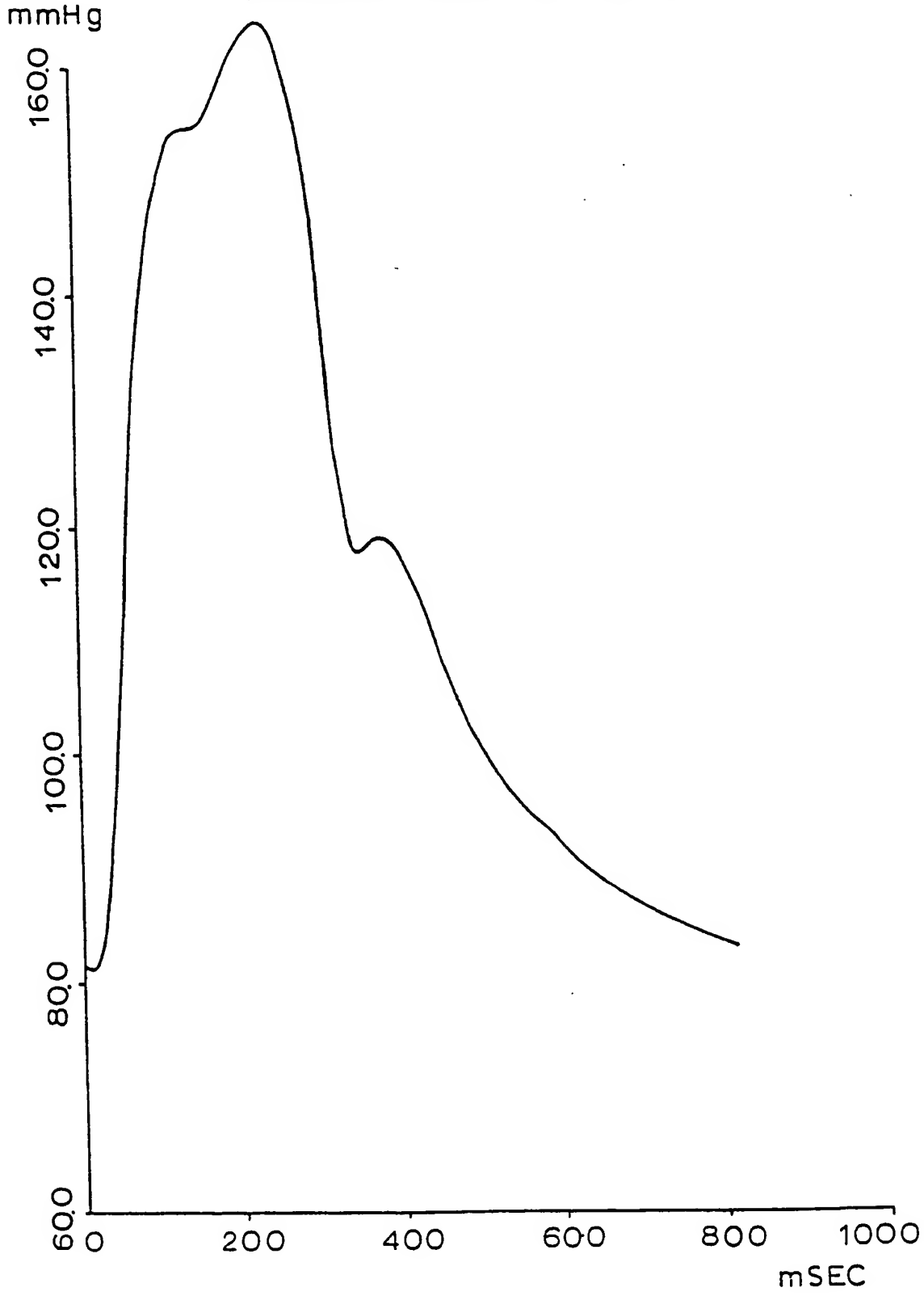


FIG. 20

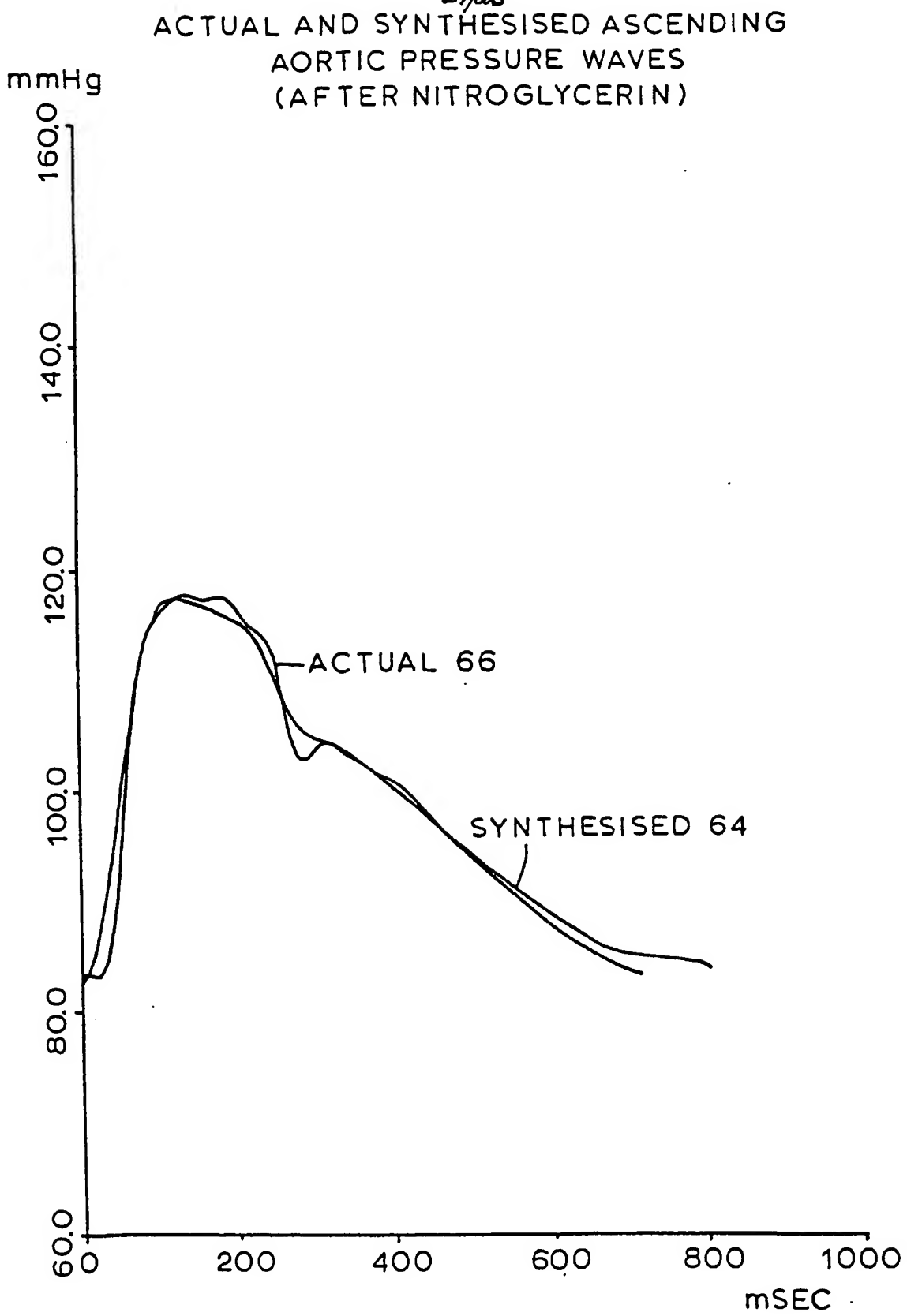

ACTUAL AND SYNTHESISED ASCENDING
AORTIC PRESSURE WAVES
(AFTER NITROGLYCERIN)
mmHg
160.0
140.0
120.0
100.0
80.0
60.0
ACTUAL 66
SYNTHESISED 64
0
200
400
600
800
1000
mSEC

FIG. 21

BRACHIAL ARTERY PRESSURE WAVE USED FOR SYNTHESIS OF ASCENDING AORTIC PRESSURE WAVE IN FIG. 20

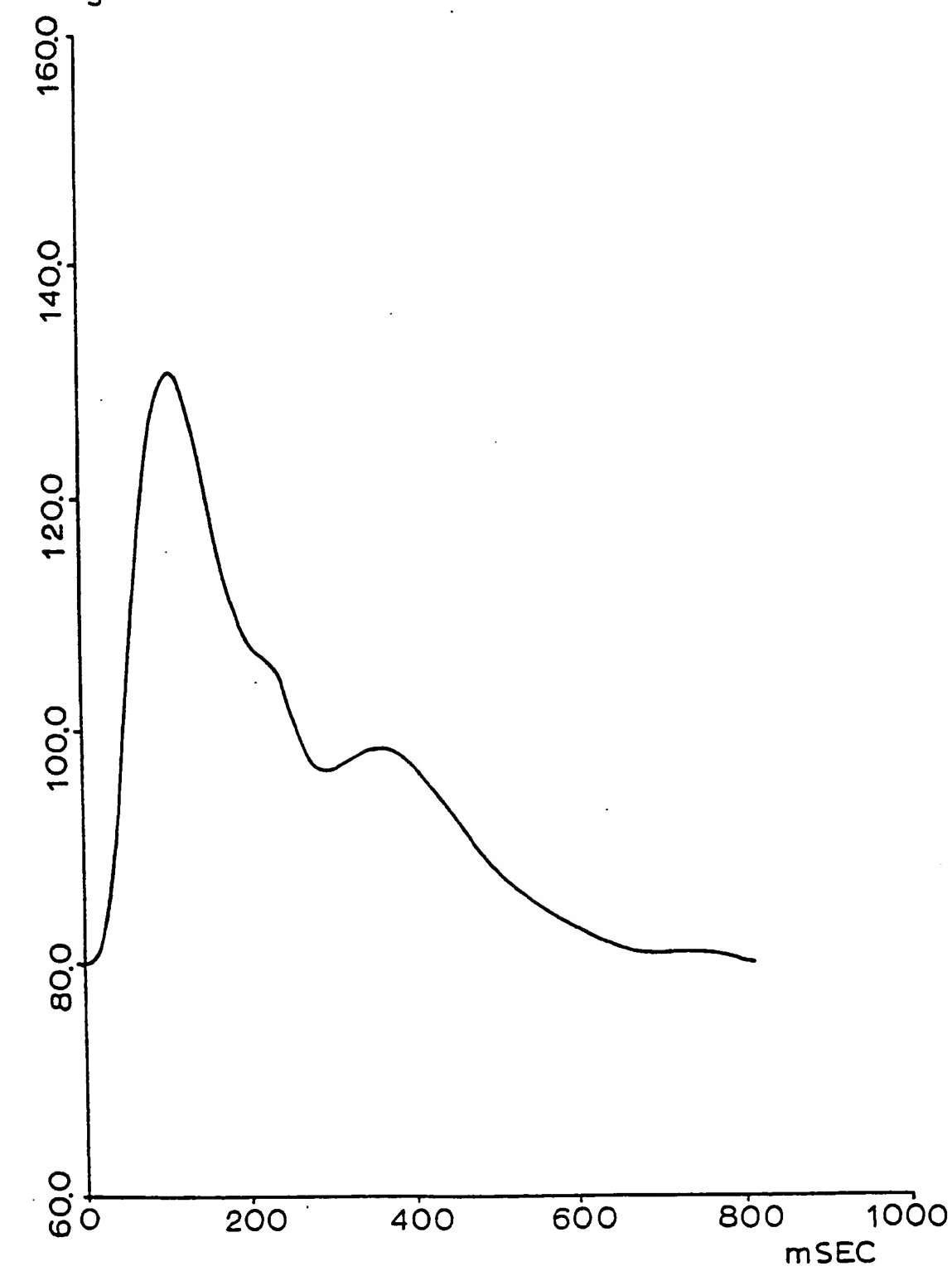


FIG. 22

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 90/01612

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 A61B5/021

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	A61B

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No.[13]
A	IEEE TRANSACTIONS ON BIO-MEDICAL ENGINEERING. vol. BME19, no. 4, July 1972, NEW YORK US pages 261 - 271; j.j. Strano et al: "Measurement and utilization of In Vivo blood-pressure transfer functions of dog and chicken aortas" see the whole document ---	1
A	MEDICAL AND BIOLOGICAL ENGINEERING AND COMPUTING. vol. 25, no. 3, May 1987, STEVENAGE GB pages 277 - 283; R. Burattini et al.: "Dynamics of the short-term regulation of arterial pressure:frequency dependence and role of arterial compliance" see the whole document ---	1

-/--

° Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
02 JULY 1990	19. 07 90
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	FERRIGNO A.

Form PCT/ISA/210 (second sheet) (January 1985)

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	SCANDINAVIAN JOURNAL CLIN. LAB. INVEST. vol. 33, 1974, pages 371 - 377; P.E.NIELSEN ET AL.: "Systolic pressure amplification in the arteries of normal subjects" see the whole document ---	1